# Efficacy Outcomes in Clinical Trials of Atopic Dermatitis Treatments: A Systematic Literature Review

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## INTRODUCTION

- Complete skin clearance is a key atopic dermatitis (AD) treatment goal[1,2]
- Treatment efficacy in AD trials is evaluated using a range of clinical measures, with the Investigator Global Assessment (IGA) as a key endpoint[3,4]
- Multiple forms of the IGA scale have been utilized across trials; these include the Investigator Static Global Assessment (ISGA) and the Validated Investigator Global Assessment for AD™ (vIGA-AD™)[3,4]
  - IGA scale scores usually range from 0 (clear) through to 1 (almost clear), 2 (mild), 3 (moderate), and 4 (severe), but may contain differences (e.g. in definitions, level of detail, or response options)[4]
- Efficacy endpoints using IGA scales include achieving IGA=0 or 1 with ≥2-grade improvement from baseline or achieving IGA=0[3]
- Achievement of IGA=0 or 1 with ≥2-grade improvement or ≥75% improvement from baseline in Eczema Area and Severity Index (EASI) score (EASI75) are commonly used regulatory endpoints that have clinical significance[5,6]
- Recently, more stringent endpoints have been utilized, including achieving IGA=0 or ≥90% improvement in EASI score (EASI90), which may be more clinically useful outcome measures
- Differences in the use of these endpoints across AD trials and trial populations have not been well described

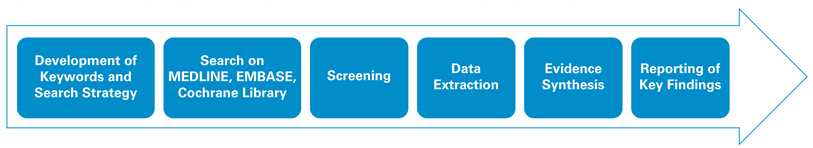
## OBJECTIVE

- To compare differences in published efficacy outcomes in recent clinical trials of FDA-approved AD treatments for adults and children

## MATERIALS AND METHODS

- A systematic literature search was conducted using MEDLINE, Embase, Cochrane Library databases, and hand searches
- The search identified randomized, single-arm, and open-label trials in patients with mild, moderate, and severe AD published between January 1, 2016 and August 16, 2023 (full manuscript publications) or August 16, 2022 and August 16, 2023 (congress abstracts)
- Trials could include patients with any severity of AD
- Trial treatments were agents that had been recently FDA approved for AD:
  - Topical therapies: Crisaborole or ruxolitinib
  - Injectable systemics: Dupilumab or tralokinumab
  - Oral systemics: Upadacitinib or abrocitinib
- Efficacy data included endpoints:
  - IGA=0 or 1 and ≥2-grade-improvement from baseline and IGA=0 (measured using IGA, ISGA, or vIGA-AD™)
  - Achievement of EASI75 and EASI90
- Efficacy data measures were categorized and summarized by:
  - Disease severity: Mild, moderate, or severe, and groupings of severities as reported by the trials
  - Treatment type: Topical therapies, injectable systemics, or oral systemics
  - Patient age groups: <12 years (children), 12–17 years (adolescents), ≥12 years (adolescents and adults), and ≥18 years (adults)
- The searches and reporting of data followed the standards for Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)[7] (**Figure 1**)

**Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)***



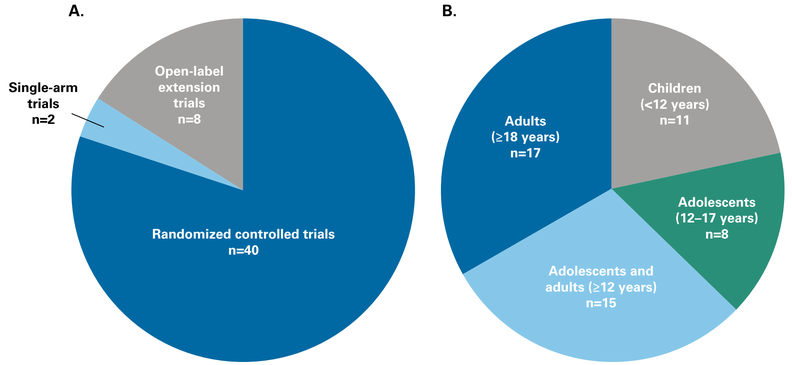

*A summary of PRISMA is shown.

## RESULTS

### Identified Publications

- The systematic literature search identified 50 publications that reported trial data with the selected efficacy outcomes and recently FDA-approved AD treatments
  - Four publications were for trials in the US only, and 46 publications were for global trials (multiple countries, including US sites)
- Of 50 publications identified, 40 (80%) were randomized controlled trials, 2 (4%) were single-arm trials, and 8 (16%) were open-label extension trials (**Figure 2A**)
- By age group, 17/50 trials (34%) included only adults (age ≥18 years) (**Figure 2B**)
- Moderate to severe AD was the AD severity studied most frequently in 38/50 (76%) of publications
  - All these trials evaluated either systemic monotherapy or systemic therapy combined with a topical agent
- Trials of topical monotherapy for mild to moderate AD only were reported in 8/50 (16%) publications

**Figure 2. (A) Types of Trials and (B) Population Age Groups Identified by the Systematic Literature Search**




### Number of Publications for Baseline AD Severities by Type of AD Treatment and Key Efficacy Endpoints Reported

- For topical therapies (**Table 1**):
  - No trials reported endpoints in patients with moderate to severe AD
  - No trials reported IGA/ISGA/vIGA-AD™=0 (complete disease clearance)
- For injectable or oral systemics, there were no trials evaluating patients with mild to moderate AD (**Table 1**)

**Table 1. Number of Publications for Baseline AD Severities by Type of AD Treatment and Key Efficacy Endpoints Reported**

| Number of publications reporting trial endpoint, n | AD severity | | |
|---|---|---|---|
| | Mild to moderate | Moderate to severe | Severe |
| **Topical therapies (crisaborole or ruxolitinib)** | | | |
| IGA=0 or 1 and ≥2-grade improvement | 4 | 0 | 0 |
| IGA=0 | 0 | 0 | 0 |
| EASI90 | 3 | 0 | 0 |
| EASI75 | 2 | 0 | 0 |
| **Injectable systemics (dupilumab or tralokinumab)** | | | |
| IGA=0 or 1 and ≥2-grade improvement | 0 | 9 | 2 |
| IGA=0 | 0 | 4 | 0 |
| EASI90 | 0 | 17 | 1 |
| EASI75 | 0 | 15 | 2 |
| **Oral systemics (upadacitinib or abrocitinib)** | | | |
| IGA=0 or 1 and ≥2-grade improvement | 0 | 10 | 0 |
| IGA=0 | 0 | 3 | 0 |
| EASI90 | 0 | 20 | 0 |
| EASI75 | 0 | 15 | 0 |

The total number of publications shown may be >50 because a publication could report endpoints for more than one AD severity category.
The IGA category includes trials that evaluated this endpoint using the IGA, ISGA, or vIGA-AD™ scales.
AD, atopic dermatitis; EASI, Eczema Area and Severity Index; EASI75 or EASI90, ≥75% or ≥90% improvement in EASI score from baseline; IGA, Investigator Global Assessment; ISGA, Investigator Static Global Assessment; vIGA-AD™, Validated Investigator Global Assessment for Atopic Dermatitis™.

### Number of Publications for Trial Population Age Groups by Type of AD Treatment and Key Efficacy Endpoints Reported

- For topical therapies (**Table 2**):
  - No trials reported achievement of IGA=0 (complete disease clearance) for any age group
  - Achievement of EASI90 was not reported for children aged <12 years in any trials
- For injectable systemics, no trials reported evaluating IGA=0 (complete disease clearance) in children aged <12 years (**Table 2**)
- For oral systemics, there were no trials evaluating outcomes in children aged <12 years (**Table 2**)

**Table 2. Number of Publications for Trial Population Age Groups by Type of AD Treatment and Key Efficacy Endpoints Reported**

| Number of publications reporting trial endpoint, n | Patient age group | | | |
|---|---|---|---|---|
| | Children (<12 years) | Adolescents (12–17 years) | Adolescents and adults (≥12 years) | Adults (≥18 years) |
| **Topical therapies (crisaborole or ruxolitinib)** | | | | |
| IGA=0 or 1 and ≥2-grade improvement | 3 | 2 | 2 | 1 |
| IGA=0 | 0 | 0 | 0 | 0 |
| EASI90 | 0 | 0 | 3 | 0 |
| EASI75 | 1 | 0 | 2 | 0 |
| **Injectable systemics (dupilumab or tralokinumab)** | | | | |
| IGA=0 or 1 and ≥2-grade improvement | 3 | 2 | 0 | 6 |
| IGA=0 | 0 | 1 | 0 | 3 |
| EASI90 | 2 | 3 | 0 | 13 |
| EASI75 | 4 | 2 | 0 | 11 |
| **Oral systemics (upadacitinib or abrocitinib)** | | | | |
| IGA=0 or 1 and ≥2-grade improvement | 0 | 2 | 6 | 2 |
| IGA=0 | 0 | 0 | 2 | 1 |
| EASI90 | 0 | 4 | 11 | 6 |
| EASI75 | 0 | 4 | 8 | 5 |

The total number of publications shown may be >50 because a publication could report endpoints for more than one patient age group category.
The IGA category includes trials that evaluated this endpoint using the IGA, ISGA, or vIGA-AD™ scales.
AD, atopic dermatitis; EASI, Eczema Area and Severity Index; EASI75 or EASI90, ≥75% or ≥90% improvement in EASI score from baseline; IGA, Investigator Global Assessment; ISGA, Investigator Static Global Assessment; vIGA-AD™; Validated Investigator Global Assessment for Atopic Dermatitis™.

## CONCLUSIONS

- This systematic literature search of AD trial publications from 2016 onwards on therapies recently approved by the FDA revealed several gaps in available efficacy outcomes data
- No trials assessed a topical therapy for moderate to severe AD, and complete disease clearance (IGA=0) was not reported for any topicals
- There were no trial publications of oral systemic therapies in children aged <12 years
- These findings reinforce the unmet need for AD treatment options that can provide efficacy for all patients regardless of age and severity

## REFERENCES

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