Dermatology Practical & Conceptual

Tapinarof Versus Crisaborole for Pediatric Atopic Dermatitis: A Systematic Review and Meta-Analysis

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ABSTRACT

Introduction: A chronic inflammatory skin ailment marked by pruritus and eczematous lesions, atopic dermatitis (AD) greatly lowers patient quality of life. Alternatives to corticosteroids have surfaced in nonsteroidal topical medicines such crisaborole and tapinarof, which provide focused anti-inflammatory effects with fewer general adverse effects.

Objective: The aim of this systematic review and meta-analysis was to assess and compare the safety and efficacy profiles of crisaborole and tapinarof in the management of mild-to-moderate AD.

Methodology: A search of several databases produced 510 studies; after removing duplicates and applying eligibility criteria, 24 studies, including a pooled sample of 8,218 patients (average age 17.5 years), were included. Using the Investigator's Static Global Assessment (ISGA) and Eczema Area and Severity Index (EASI), efficacy outcomes were evaluated; safety was based on incidence of adverse events.

Results: Among 1,164 patients receiving crisaborole, 61% (95% CI: 44–76%) achieved ISGA 0–1; In the tapinarof group, 49% (95% CI: 43–55%) achieved the outcome, with no statistically significant difference observed ($\chi^2 = 1.70$, P = 0.192).Similarly, 60% (95% CI: 55–65%) of crisaborole patients and 66% (95% CI: 53–82%) of those on tapinarof showed EASI improvement with no significant variation (chi=1.11, *P*=0.293). In the tapinarof group, 49% (95% CI: 43–55%) achieved the outcome, with no statistically significant difference observed ($\chi^2 = 1.70$, P = 0.192). Rare severe events and therapy discontinuation occurred for both drugs.

Conclusion: Mild-to-moderate AD may be effectively and safely managed with either crisaborole or tapinarof. With no major efficacy or safety differences, treatment choice can be guided by patient preference, tolerability, and clinical context.

Introduction

With an increasing prevalence in both developed and underdeveloped countries, atopic dermatitis (AD) is a chronic, relapsing inflammatory skin disease affecting up to 20% of children worldwide [1,2]. Marked by pruritus, xerosis, and eczematous lesions, pediatric AD greatly impairs quality of life for patients and their families, frequently causing sleep problems, behavioral problems, and increased psychological strain [3,4]. The pathogenesis of atopic dermatitis is multifactorial; it results from a complicated interaction between genetic predisposition, skin barrier dysfunction, immune dysregulation, and environmental triggers [5,6].

Traditional treatment of AD in youngsters include emollients, topical corticosteroids (TCS), and calcineurin inhibitors [7-9]. Concerns about long-term safety, especially with TCS, have nevertheless led to a demand for steroid-sparing substitutes with good safety profiles and long-lasting efficacy [7]. In recent years, newer non-steroidal topical agents such tapinarof and crisaborole have shown to be promising therapies for mild-to-moderate AD [10, 11].

An aryl hydrocarbon receptor (AhR) agonist, tapinarof modulates inflammatory pathways and stimulates skin barrier repair [12]. It has shown to be successful in both adult and juvenile populations; Phase 3 studies reveal significant decrease in disease severity and tolerability [13]. Conversely, a topical phosphodiesterase-4 (PDE-4) inhibitor licensed for pediatric use, crisaborole exerts its anti-inflammatory effect by lowering cyclic AMP degradation and decreasing pro-inflammatory cytokines [13]. While well-tolerated and effective in children, some patients experience localized irritation and varying treatment response [13].

Direct comparison of tapinarof's effectiveness and safety in pediatric AD is justified to guide clinical decision-making given crisaborole's established role and tapinarof's recent emergence. Although both medications are non-steroidal and authorized for use in children, differences in mechanism of action, onset of alleviation, and adverse event profiles may affect treatment choice.

This systematic review and meta-analysis mainly aimed to assess the effectiveness and safety of tapinarof as opposed to crisaborole in the treatment of pediatric atopic dermatitis. Specific results are improvements in disease severity (e.g., EASI, IGA scores), patient-reported measures (e.g., pruritus and quality of life), and incidence of adverse events. Through synthesizing data from existing randomized controlled trials and observational studies, this review seeks to offer a complete comparison to assist evidence-based management of pediatric AD.

Methods

To guarantee methodological rigor and transparency, this systematic review and meta-analysis was carried out under PRISMA rules. A thorough literature search was carried out across several electronic databases, including PubMed, ScienceDirect, Wiley Online Library, Web of Science (WoS), Google Scholar, Scopus, Medline, the Cochrane Library, and ClinicalTrials.gov. A mix of medical subject headings (MeSH) and free-text terms pertaining to the population, intervention, and outcomes of interest was used to carry out the search. Key search terms included: atopic dermatitis, pediatric eczema, tapinarof, crisaborole, non-steroidal therapy, eczema treatment, inflammatory skin condition, topical treatment, eczema severity, patient-reported outcomes, Investigators Global Assessment (IGA), Eczema Area and Severity Index (EASI), and adverse effects. The search strategy was polished and optimized using Boolean operators AND and OR. To only include studies published in English, filters were employed.

Defined inclusion and exclusion criteria guided the choice of qualified studies. Only randomized controlled trials (RCTs), observational studies, cohort studies, case-control studies, cross-sectional studies, and case series were considered for inclusion if they evaluated the effectiveness and/or safety of tapinarof or crisaborole in children diagnosed with atopic dermatitis. Studies lacking particular data on pediatric groups were excluded, as were systematic reviews, meta-analyses, in vitro or in vivo animal trials. Studies had to disclose at least one of the following outcomes: EASI, IGA, Dermatology Life Quality Index (DLQI), patient-reported symptoms, or adverse events.

Two reviewers independently carried out data extraction using a standardized data extraction form. The extracted data included study characteristics such as the study ID (based on the last name of the first author and year of publication), year of publication, study design, and sample size. Patient characteristics such mean age, sex distribution, baseline disease severity (categorized as mild, moderate, or severe), inclusion and exclusion criteria, and presence of comorbidities (e.g., asthma, allergic rhinitis, food allergies) were also collected. The intervention was thoroughly documented, with

the dose and method of tapinarof and crisaborole administration, duration of treatment, and claimed compliance to treatment guidelines noted.

Outcomes measures included changes in EASI and IGA scores, patient-reported outcomes such as quality of life assessments, and the frequency and nature of adverse effects, including local skin reactions (e.g., burning, stinging, hypersensitivity). Specific data on adverse effects were gathered separately for both tapinarof and crisaborole, and any reports of long-term safety concerns were documented. Follow-up data were collected when available, including the duration of follow-up after treatment cessation, sustainability of improvements in disease severity, and any long-term dermatological or systemic effects.

Using the Cochrane Risk of Bias tool, which assesses domains including randomization, blinding, outcome reporting, and missing data, the risk of bias for each randomized controlled trial was evaluated. For non-randomized comparative research, the ROBINS-I instrument was used to evaluate possible confounding, selection bias, and measurement bias. Furthermore, the Newcastle-Ottawa Scale (NOS) was applied to grade the quality of included case-control and cross-sectional investigations based on selection, comparability, and exposure or outcome evaluation. Any disagreements between reviewers during study selection, data extraction, or quality evaluation were addressed through discussion or third review.

Results

General Characteristics of the Studies

The search of several databases across the literature yielded 510 studies, of which 213 were removed owing to duplication. The remaining 297 studies were assessed for eligibility; 271 studies were eliminated based on their title and abstract, failure to provide sufficient data for analysis, lack of complete access to the full study, or wrong population. This produced 25 papers analyzed for this review.

The present review was carried out on 25 studies (Figure 1, [13,15-38]) totaling 8,218 patients with mean age of 17.5 years (standard deviation=9.77). The sex distribution was somewhat equal across studies where the pooled frequency of male sex was 39.6%. Baseline disease severity varied; Investigator's Static Global Assessment (ISGA) scores ranged from 1.5 to 13.22, reflecting a spectrum of disease severities. Eczema Area and Severity Index (EASI) scores, where reported, indicated mild-to-moderate AD in most cohorts (Table 1).

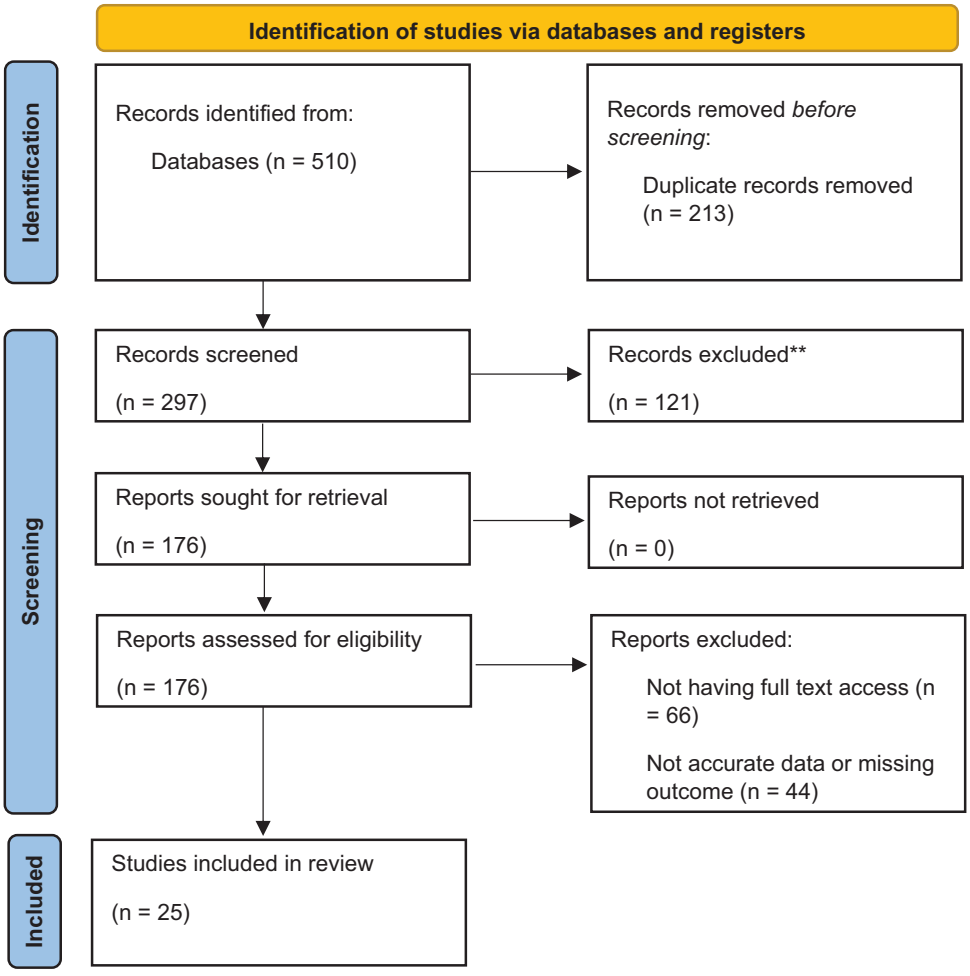

Figure 1. PRISMA flow diagram for study inclusion.

Table 1. General characteristics of the studies.

Study ID	Study Design	Country of Study	Total Sample Size	Age, Mean (SD, Range)	Sex, Male, N (N%)	ISGA	IGA	BSI	EASI
Yang, 2025 [17]	Randomized controlled trial	China	142	3.12 (NA, 2-16)	65 (45.7 %)	NA	2.51 (0.56)	NA	6.75 (4.11)
Stein Gold, 2025 [19]	Randomized, double blind	USA	813	15.6 (16.6, 2-81)	370 (45.5 %)	NA	Moderate (83.5-90.4%)	NA	12.2 (5.0)
Simpson, 2025 [32]	Randomized, double-blind	USA	813	15.6 (16.6, 2-18)	247 (30.4%)	Moderate (83.7-90.4%)	NA	15.8%	12.2 (5.0)
De, 2024 [15]	Open-label prospective study	India	19	6.52 (4.22, 2-16)	12 (63.3%)	2.58 (0.61)	NA	2.32 (0.48)	NA
Chakraborty, 2024 [18]	Randomized controlled trial	India	40	NA (NA, >2 years)	NA	NA	NA	NA	NA
Silverberg, 2024 [13]	Randomized, double blind	USA and Canada	813	15.6 (16.6, 2-81)	130 (15.9%)	NA	NA	NA	12.2 (5.0)
Igarashi, 2024 [25]	Randomized, double-blind	Japan	121	7 (2.6, 2-11)	66 (54.5%)	NA	NA	NA	11.2 (4.1)
Ryan Wolf, 2024 [30]	Cross -sectional clinical trial	USA	47	8 (3.9, 2-15)	19 (40.4%)	Moderate (20%)	NA	13.9%	4.9 (3.7)
Eichenfield, 2024 [37]	Randomized, double-blind	Multinational (includes USA, Canada, Israel, Taiwan, UK, Brazil)	270	NA (NA, >3months)	131 (48.5%)	0.6 (NA)	NA	5.20%	1.5 (2.1)
Eichenfield, 2023 [33]	Randomized, double-blind	Multi-national (USA, Canada, China, Australia, UK)	270	22.2 (2.2, 3-18)	123 (45.6%)	Moderate (60 %)	NA	5.46%	1.67 (2.22)
Ma, 2023 [16]	Randomized, double-blind, vehicle-controlled phase 3 clinical trial	China and Japan	391	18.3 (15.8, NA)	205 (52.4 %)	Mild (42.5%)	NA	NA	10.2 (7.0)
Paller, 2021 [22]	Randomized, double-blind	USA, Canada, Japan	247	NA (NA, 12-65)	NA	NA	Moderate (91 %)	NA	11.3 (6.0)

Fujita1, 2021 [26]	Randomized, double-blind	Japan	81	33.6 (10.4, 2-55)	47 (58.0%)	2.4 (0.5)	NA	NA	NA
Geng, 2021 [36]	open-label, long-term extension study	Global	418	11.7 (NA, 2-30)	175 (41.9%)	2.1-2.7	NA	NA	NA
Silverberg, 2020 [31]	Randomized, double-blind	USA	1522	12.3 (12.16, 2-79)	450 (29.6%)	2.6 (0.49)	NA	18.3%	NA
Schlessinger, 2020 [34]	Open-label, single-arm Phase IV trial	USA, Canada, Australia	137	13.6 (6.42, 3-24) months	88 (64.2%)	2.6 (0.5)	NA	28.1%	11.8 (8.41)
Bissonnette, 2019 [20]	Randomized controlled trial	Canada	40	32.2 (NA, NA)	13 (32.5%)	Moderate (87.5%)	NA	NA	NA
Peppers, 2019 [23]	Randomized, double-blind	USA, Canada, and Japan	247	29.3 (14.83, 12-65)	126 (51.0%)	NA	3.1 (NA)	16.9%	11.25 (5.96)
Ono, 2019 [28]	Randomized, vehicle-controlled	Japan	32	33.1 (11.24, 22-55)	32 (100%)	Moderate (83.3%)	NA	63.9%	NA
Bissonnette, 2018 [27]	Cohort	Canada	11	31.6 (10.55,21-54)	8 (72.7%)	NA	3.4 (0.5)	NA	13.22 (4.1)
Simpson, 2018 [35]	Randomized, double-blind	USA	1016	NA (NA, 2-30)	675 (66.4%)	NA	NA	NA	NA
Eichenfield, 2017 [21]	Open-label, single-arm, long-term safety study	USA	517	11.7 (10.39, 2-72)	211 (40.8%)	NA	NA	18%	NA
Zane, 2016 [24]	Open label, non-randomized	USA	34	9.3 (4.54, 2-17)	15 (44.1%)	2.65 (0.49)	NA	48.7%	NA
Tom, 2016 [29]	Randomized controlled trial	USA	23	15 (1.5, 12.1-17.3)	4 (17.4%)	2.43 (0.51)	NA	18%	NA

Intervention Characteristics

The interventions assessed included tapinarof and crisaborole, administered topically with varying concentrations and frequencies. Fourteen studies assessed the efficacy and safety of crisaborole [15-18,21,24,26,28,31,34-37], while ten studies assessed tapinarof [13, 19, 20,22,23,25,27,29,32,33] and two studies assessed both of crisaborole and tapinarof [19,30]. Crisaborole was predominantly applied at a 2% concentration twice daily over durations ranging from eight to 364 days. Tapinarof was administered at concentrations of between 0.5% and 2%, with application frequencies ranging from once to twice daily over periods of eight to 84 days. Concomitant treatments varied, with some studies permitting the use of emollients, moisturizers, and corticosteroids, while others restricted additional therapies to isolate the effects of the study drugs (Table 2).

Table 2. General characteristics of the interventions.

Study ID	Intervention	Dose and Frequency per day	Duration (days)	Route of Administration	Concomitant Treatment
Yang, 2025 [17]	Crisaborole	2%, Twice	112	Topical	Topical antibiotics, oral antihistamines
Stein Gold, 2025 [19]	Tapinarof	1%, once	56	Topical	Not allowed
Simpson, 2025 [32]	Tapinarof	1%, once	56	Topical	NA
De, 2024 [15]	Crisaborole	2 %, Twice		Topical	Oral antihistamines and inhaled corticosteroids, bland emollients
Chakraborty, 2024 [18]	Crisaborole	2%, Twice	28	Topical	NA
Silverberg, 2024 [13]	Tapinarof	1%, once	56	Topical	Topical emollients
Igarashi1, 2024 [25]	Tapinarof	0.5-1%, once	56	Topical	Not allowed
Ryan Wolf, 2024 [30]	Tapinarof, Crisaborole	2% Twice, 2% twice	84, 84	Topical	Antihistamines and/or topical corticosteroids
Eichenfield, 2024 [37]	Crisaborole	%, Twice	364	Topical	NA
Eichenfield, 2023 [33]	Crisaborole	2%, once	364	Topical	Topical emollients
Ma, 2023 [16]	Crisaborole	2%, Twice	28	Topical	Emollients, moisturizers, and sunscreen
Paller, 2021 [22]	Tapinarof	0.5-1%, once or twice	84	Topical	Not allowed
Fujita1, 2021 [26]	Crisaborole	2%, once	14	Topical	Topical emollients, moisturizers, topical corticosteroids/calcineurin inhibitors
Geng, 2021 [36]	Crisaborole	2%, Twice	28	Topical	Low-to-mid potency topical corticosteroids or calcineurin inhibitors, Bland emollients
Silverberg, 2020 [31]	Tapinarof	2%, Twice	28	Topical	NA
Schlessinger, 2020 [34]	Crisaborole	2%, Twice	28	Topical	Bland emollients
Bissonnette, 2019 [20]	Tapinarof	2%, Twice	42	Topical	Topical emollients
Peppers, 2019 [23]	Tapinarof	0.5-1%, once or twice	84	Topical	Not allowed
Ono, 2019 [28]	Crisaborole	2%, Twice	8	Topical	Not allowed
Bissonnette, 2018 [27]	Tapinarof	1-2%, twice	21	Topical	NA
Simpson, 2018 [35]	Crisaborole	2%, Twice	28	Topical	NA
Eichenfield, 2017 [21]	Crisaborole	2%, Twice	43.4	Topical	Not allowed
Zane, 2016 [24]	Crisaborole	2%, Twice	28	Topical	Oral antihistamine, topical retinoids
Tom, 2016 [29]	Tapinarof	2%, Twice	28	Topical	Emollients on non-treated areas

Clinical Outcomes

Efficacy outcomes were primarily measured using ISGA and EASI scores. Crisaborole demonstrated significant improvements, with ISGA 0–1 achievement rate ranging from 40% to 77.6% across studies. EASI score reductions were also notable, with Ma et al. (2023) reporting a 59.9% improvement [16]. Tapinarof showed comparable efficacy, with an ISGA 0–1 rate of between 32.5% and 53%, and EASI score reductions up to 81.29% as observed in Igarashi et al. [25]. Time to response varied, with improvements noted as early as day 2 in some studies, and most participants experiencing significant relief by day 14. Quality of life measures, including the Children's Dermatology Life Quality Index (CDLQI) and Patient-Oriented Eczema Measure (POEM), indicated substantial improvements, particularly with tapinarof treatment (Table 3).

Meta-analysis was conducted among 10 studies (six among patients on crisaborole, and four for tapinarof) to assess the prevalence of patients achieving ISGA 0-1. The

Table 3. Outcomes.

Study ID	Intervention	ISGA 0–1	EASI	Relapse	Time to Response or Improvement (days)	Quality of Life Measures (CDLQ, POEM)	Types of AEs (Local reaction, systemic reactions)
Yang, 2025 [17]	Crisaborole	NA	NA	43.84%	56.65 (23.97)	NA	URTIs, diarrhea, abdominal pain, etc. (unrelated to treatment)
Stein Gold, 2025 [19]	Tapinarof	45.40%	55.8%	NA	28	NA	Local burning, stinging, itching (slight)
Simpson, 2025 [32]	Tapinarof	NA	NA	NA	7	CDLQI: -6.8	Folliculitis, headache, nasopharyngitis
De, 2024 [15]	Crisaborole	14 (73.7%)	NA	NA	8	CDLQI: reduced from 13.79 ± 3.57 to 6.74 ± 1.97	Local reactions (burning); no systemic reactions
Chakraborty, 2024 [18]	Crisaborole	Improved significantly	NA	NA	8	CDLQI: reduced from 13.79 to 6.74	Irritation
Silverberg, 2024 [13]	Tapinarof	NA	45.4%	NA	NA	NA	Folliculitis, headache, nasopharyngitis (mild/ moderate)
Igarashi, 2024 [25]	Tapinarof	NA	81.29%	NA	7	NA	Local application site irritation, contact dermatitis and Systemic gstroenteritis, nasopharyngitis, headache
Ryan Wolf, 2024 [30]	Tapinarof, Crisaborole	NA	EASI decreased from 4.9 to 3.0 and 4.8 to 2.4	NA	42	CDLQI: 9.4 ± 6.0 vs 5.8 ± 5.1	Local Burning sensation
Eichenfield, 2024 [37]	Crisaborole	64%	NA	NA	41.5	NA	Local flares

Table 3 continues

Table 3. Outcomes. *(continued)*

Study ID	Intervention	ISGA 0–1	EASI	Relapse	Time to Response or Improvement (days)	Quality of Life Measures (CDLQ, POEM)	Types of AEs (Local reaction, systemic reactions)
Eichenfield, 2023 [33]	Crisaborole	NA	NA	NA	NA	NA	URTIs, influenza, skin abrasions, COVID-19, and headache.
Ma, 2023 [16]	Crisaborole	41.40%	59.90%	NA	28	PP-NRS (pruritus): -1.58	Application site pain
Paller, 2021 [22]	Tapinarof	53%	NA	NA	7	POEM Scores: Improvement across most symptoms	Local application-site irritation, burning, stinging
Fujita1, 2021 [26]	Crisaborole	NA	NA	NA	2	NA	Local application site irritation, Systemic Oropharyngeal pain, Hand-foot-and-mouth disease (isolated)
Geng, 2021 [36]	Crisaborole	77.60%	NA	NA	28	NA	viral URTIs, cough, and atopic dermatitis
Silverberg, 2020 [31]	Tapinarof	NA	NA	NA	8	CDLQI: 9.3 (5.99)	NA
Schlessinger, 2020 [34]	Crisaborole	NA	NA	NA	8	NA	Application site pain, discomfort, erythema, pyrexia, URTIs, diarrhea
Bissonnette, 2019 [20]	Tapinarof	NA	NA	NA	1	NA	Mild application site pain, pruritus)
Peppers, 2019 [23]	Tapinarof	53%	NA	NA	14	NA	Nasopharyngitis, Folliculitis, Atopic dermatitis (flare), URTIs, Headache, Acne, Impetigo
Ono, 2019 [28]	Crisaborole	40%	NA	NA	NA	NA	Application site irritation, Application site pain, Eyelid edema
Bissonnette, 2018 [27]	Tapinarof	NA	100%	NA	3	NA	Headache, Folliculitis, Diarrhea, nausea, vomiting
Simpson, 2018 [35]	Crisaborole	NA	NA	NA	29	NA	NA
Eichenfield, 2017 [21]	Crisaborole	NA	NA	NA	NA	NA	Atopic dermatitis, site pain, site infection

Study ID	Intervention	ISGA 0–1	EASI	Relapse	Time to Response or Improvement (days)	Quality of Life Measures (CDLQ, POEM)	Types of AEs (Local reaction, systemic reactions)
Zane, 2016 [24]	Crisaborole	64.70%	NA	NA	5	NA	Local application site pain, paresthesia, AD flare
Tom, 2016 [29]	Tapinarof	8 (34.8%)	NA	NA	8	NA	Application site pain, nasopharyngitis, application site discomfort/ dermatitis

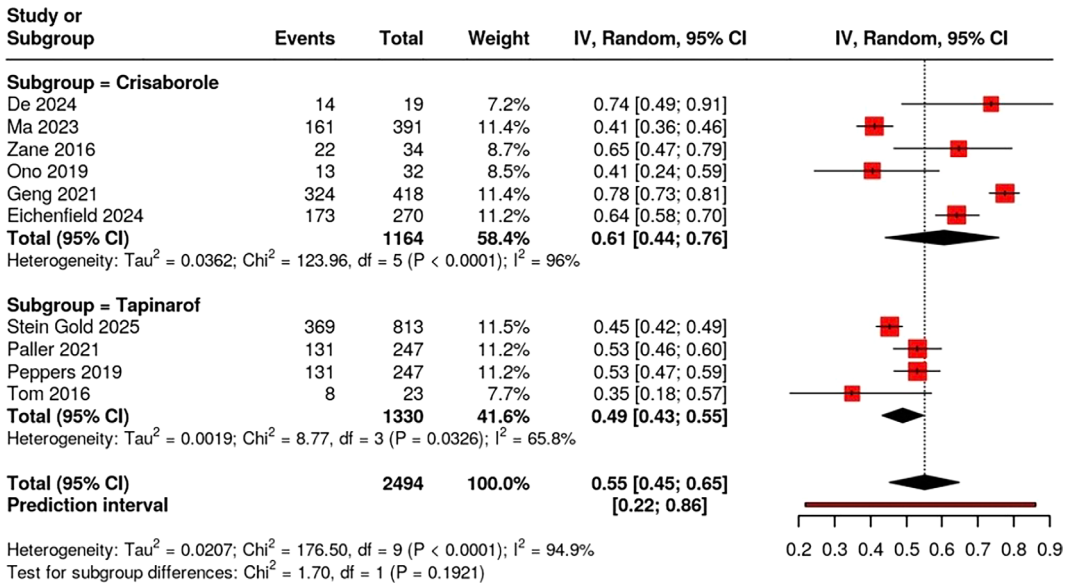

Figure 2. The difference in achieving ISGA 0–1 between patients on crisaborole and on tapinarof.

results showed that among the 1164 patients on crisaborole and 1330 patients on tapinarof, 61% (95% Confidence interval (CI): 44–76 %) and 49 % (95% CI: 43–55), respectively, achieved ISGA 0–1, with no significant difference between the two medications (chi^2=1.70, *P*=0.192). However, a significant heterogeneity was reported among studies (I^2=94.9%, *P*<0.001) (Figure 2).

In addition, the meta-analysis conducted to assess the prevalence of patients showing improvement in EASI scores indicated that among 391 patients on crisaborole and 2149 on tapinarof, 60% (95% CI: 55–65%) and 66% (95% CI: 53–82%), respectively, showed improvement, without any significant difference between the two groups (chi^2=1.11, *P*=0.293) (Figure 3).

Safety and Adverse Events

Both tapinarof and crisaborole were generally well tolerated. Common adverse events included application site reactions such as burning, stinging, and irritation. Crisaborole's most frequently reported side effect was application site pain, occurring in up to 4.4% of patients [32]. Tapinarof's adverse events were similar, with reports of folliculitis, headache, and nasopharyngitis, though these were typically mild to moderate in severity. Systemic adverse events were rare for both treatments. Notably, studies like those by Silverberg et al. [13] and Simpson et al. [32] corroborated the favorable safety profiles of these nonsteroidal topical therapies (Table 3).

In addition, the meta-analysis of the 17 studies that reported the incidence of adverse events showed an incidence of 45% (95% CI: 31–60 %) among all patients. No significant difference was found between patients on crisaborole (38%; 95 % CI: 24–52 %) and tapinarof (62%; 95% CI: 19–96%) (chi^2=1.03, *P*=0.309) (Figure 4). Moreover, both medications were associated with a very low incidence of serious adverse events (Figure 5) and low incidence of side effects associated with discontinuation of the medications (crisaborole=1%; 95% CI: 0.0–2%; tapinarof=2 %; 95% CI: 0.0–4.0 %) (Figure 6).

Risk of Bias Assessment

Overall, the majority of the randomized controlled trials demonstrated a low risk of bias, indicating robust study designs with appropriate randomization and blinding procedures. Open-label and nonrandomized studies exhibited a moderate risk of bias, primarily due to potential performance and detection biases. Cross-sectional studies assessed with the AXIS tool also showed a moderate risk, reflecting concerns related to study design and reporting. These assessments underscore the importance of rigorous methodological approaches to minimize bias and enhance the validity of study findings (Table 4).

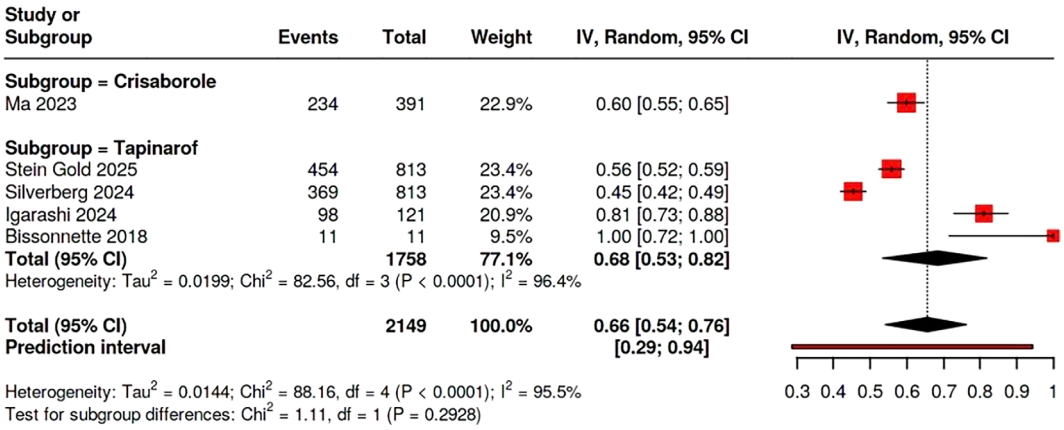

Figure 3. The difference in showing EASI improvement between patients on crisaborole and on tapinarof.

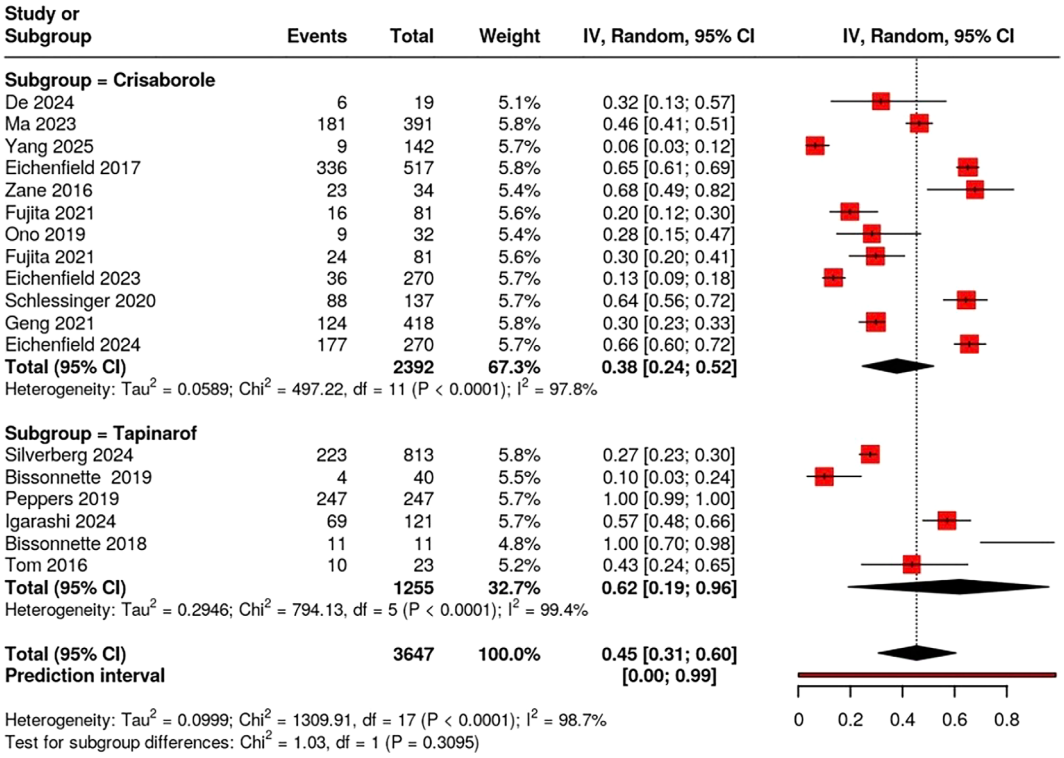

Figure 4. The difference in number of patients on crisaborole and on tapinarof with adverse events.

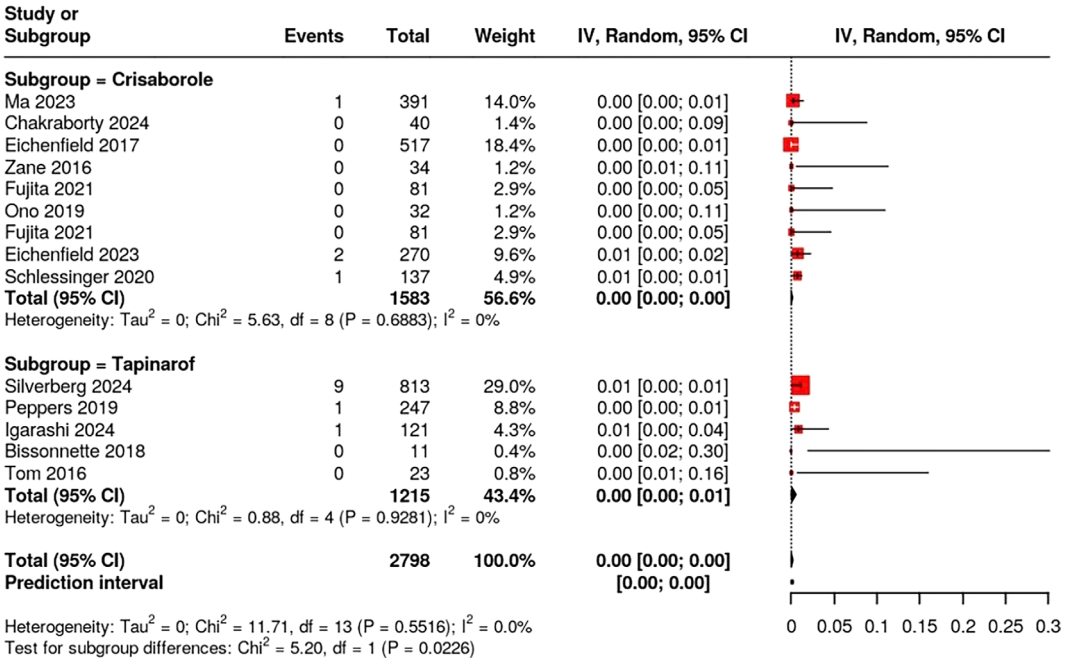

Figure 5. The difference in number of serious adverse events (SAEs) between patients on crisaborole and on tapinarof.

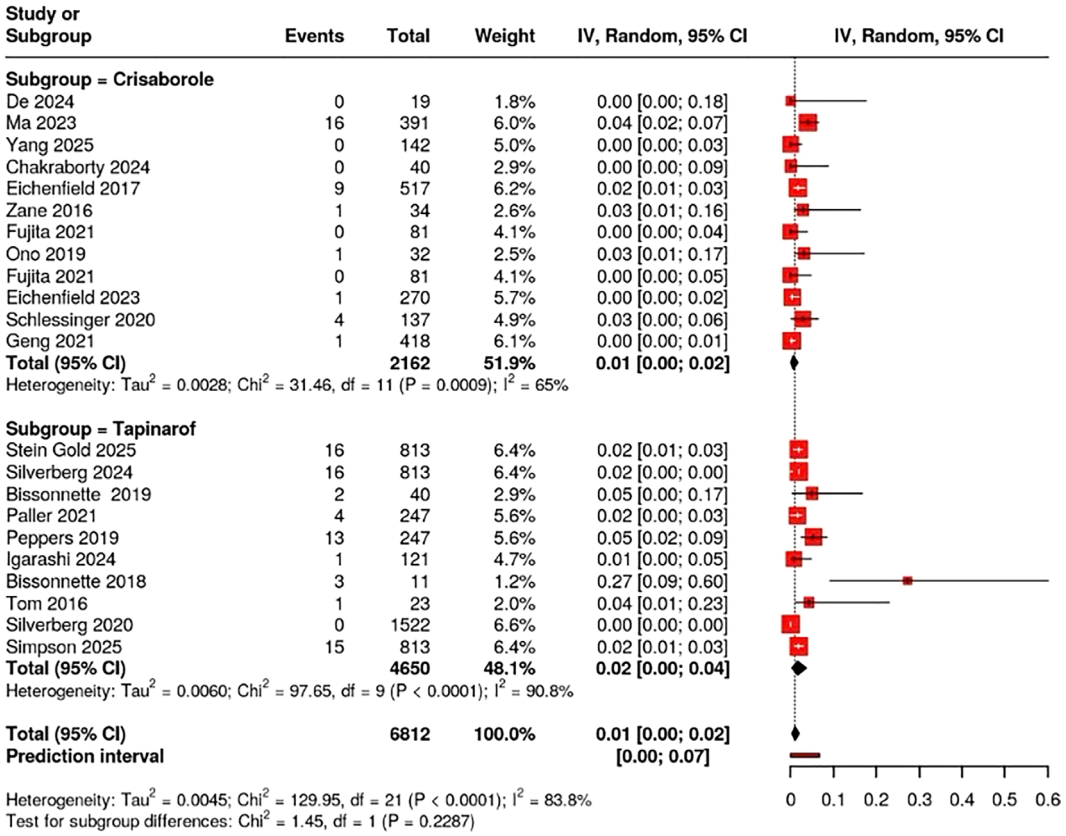

Figure 6. The difference in number of discontinuation due to AEs between patients on crisaborole and on tapinarof.

Table 4. Risk of bias assessment summary.

Study ID	Study Design	Risk of Bias Assessment Tool	Overall Risk of Bias
Yang, 2025 [17]	Randomized controlled trial	RoB 2	Low
Stein Gold, 2025 [19]	Randomized, double-blind	RoB 2	Low
Simpson, 2025 [32]	Randomized, double-blind	RoB 2	Low
De, 2024 [15]	Open-label prospective study	RoB 2	Moderate
Chakraborty, 2024 [18]	Randomized controlled trial	RoB 2	Low
Silverberg, 2024 [13]	Randomized, double-blind	RoB 2	Low
Igarashi, 2024 [25]	Randomized, double-blind	RoB 2	Low
Ryan Wolf, 2024 [30]	Cross-sectional clinical trial	AXIS	Moderate
Eichenfield, 2024 [37]	Randomized, double-blind	RoB 2	Low
Eichenfield, 2023 [33]	Randomized, double-blind	RoB 2	Low
Ma, 2023 [16]	Randomized, double-blind, vehicle-controlled phase 3 clinical trial	RoB 2	Low
Paller, 2021 [22]	Randomized, double-blind	RoB 2	Low
Fujita, 2021 [26]	Randomized, double-blind	RoB 2	Low
Geng, 2021 [36]	Open-label, long-term extension study	RoB 2	Moderate
Silverberg, 2020 [31]	Randomized, double-blind	RoB 2	Low
Schlessinger, 2020 [34]	Open-label, single-arm Phase IV trial	RoB 2	Moderate
Bissonnette, 2019 [20]	Randomized controlled trial	RoB 2	Low
Peppers, 2019 [23]	Randomized, double-blind	RoB 2	Low
Ono, 2019 [28]	Randomized, vehicle-controlled	RoB 2	Low
Bissonnette, 2018 [27]	Cohort	NOS	Moderate
Simpson, 2018 [35]	Randomized, double-blind	RoB 2	Low
Eichenfield, 2017 [21]	Open-label, single-arm, long-term safety study	RoB 2	Moderate
Zane, 2016 [24]	Open-label, nonrandomized	NOS	Moderate
Tom, 2016 [29]	Randomized controlled trial	RoB 2	Low

Discussion

The efficacy safety of two nonsteroidal topical treatments, crisaborole and tapinarof, for mild-to-moderate atopic dermatitis (AD) were assessed in this systematic review and meta-analysis of 25 studies with a combined sample size of 8,218 patients, offering a thorough summary of the performance of these drugs across various populations.

Efficacy Outcomes

Measured by the Investigator's Static Global Assessment (ISGA) and Eczema Area and Severity Index (EASI) scores, both crisaborole and tapinarof showed notable reductions in AD severity. Tapinarof demonstrated rates between 32.5% and 53%, whereas crisaborole reached ISGA 0–1 rates of between 40% and 77.6%. Ma et al. in particular found a 59.9% improvement in EASI scores with crisaborole treatment [16]. Tapinarof showed EASI score reductions up to 81.29%, as seen by Igarashi et al. [25]. These results fit with earlier research showing the efficacy of crisaborole in reducing AD symptoms [38,39].

Further supporting these results, the meta-analysis showed that 61% of patients treated with crisaborole and 49% with tapinarof attained ISGA 01, with no major difference between the two medications (chi=1.70, *P*=0.192); 60% of crisaborole-treated patients and 66% of those treated with tapinarof also showed EASI score gains, with once again no notable difference (chi=1.11, *P*=0.293). These findings indicate that both treatments have the same efficacy in controlling mild-to-moderate AD [40].

Safety and Tolerability

Generally, the safety profiles for both crisaborole and tapinarof were good. Burning, stinging, and irritation were among the most often noted adverse effects (AEs) at the application site. Crisaborole's most frequently reported AE was application site pain, affecting up to 4.4% of patients. Usually mild-to-moderate in intensity, tapinarof's AEs were similar,

with reports of folliculitis, headache, and nasopharyngitis. For both drugs, systemic AEs were uncommon, which is consistent with findings from several past studies [39,41,42].

Among all patients, a meta-analysis of 17 studies indicated an overall AE incidence of 45% (95% CI: 31–60%), with no substantial difference between crisaborole (38%; 95% CI: 24–52%) and tapinarof (62%; 95% CI: 19–96%; chi=1.03, *P*=0.309). Serious adverse events were exceedingly uncommon, and discontinuation rates as a consequence of AEs were low: 1% (95% CI: 0.02%) for crisaborole and 2% (95% CI: 0.04.0%) for tapinarof. These results support earlier research stressing the tolerance of crisaborole and tapinarof [43-45].

Clinical Implications

Crisaborole and tapinarof's similar efficacy and safety profiles give doctors latitude in customizing treatment plans for patients with mild-to-moderate AD. Patients looking for quick symptom management will particularly profit from the fast onset of action seen with both therapies, with improvements recorded as early as day 2 and considerable relief by day 14 [38,40].

Particularly with tapinarof therapy, quality of life indices like the Children's Dermatology Life Quality Index (CDLQI) and Patient-Oriented Eczema Measure (POEM) revealed significant improvements, emphasizing the need to take patient-reported outcomes into account while assessing treatment efficacy.

Limitations and Future Directions

Although this study offers insightful observations, some drawbacks should be noted. The great heterogeneity across studies (I=94.9%, *P*<0.001) indicates differences in study designs, populations, and outcome metrics, which could impact the generalizability of the results. Furthermore, the duration of treatment varied across studies (8–364 days for crisaborole and 8–84 days for tapinarof), hence maybe impacting effectiveness and safety results.

More direct comparisons will be made possible by future studies aiming to standardize outcome measures and treatment lengths. Long-term research evaluating the continued efficacy and safety of such treatments is also needed. Moreover, head-to–head investigations directly comparing crisaborole and tapinarof would offer more clear data to inform medical decision-making.

Conclusion

In conclusion, both crisaborole and tapinarof are effective and well-tolerated topical treatments for mild-to-moderate atopic dermatitis. Their same efficacy and safety profiles present doctors with practical alternatives for management of this disease. More research is needed to better define their long-term advantages and best application in varied patient populations.

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