Dermatol Ther (Heidelb)
https://doi.org/10.1007/s13555-026-01968-8

SYSTEMATIC REVIEW

Comparative Efficacy of Novel Non-steroidal Topical Therapies for Atopic Dermatitis: A Systematic Review and Network Meta-analysis

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Received: August 18, 2026 / Accepted: October 14, 2026
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ABSTRACT

***Introduction*:** Despite the availability of several non-steroidal topical therapies for atopic dermatitis (AD), their comparative speed of clinical response remains unclear. This meta-analysis compared the efficacy of novel non-steroidal topical therapies for AD.

***Methods*:** Four databases were searched for randomized controlled trials (RCTs) evaluating topical difamilast 1% twice daily (BID), tapinarof 1% once daily (QD), ruxolitinib 1.5% BID, roflumilast 0.05% or 0.15% QD in patients with AD. Outcomes included Investigator's Global Assessment Treatment Success (IGA-TS) and 50%, 75% and 90% improvement in Eczema Area and Severity Index (EASI-50, EASI-75 and EASI-90) at weeks 1, 2, 4 and 8. Frequentist random-effects network meta-analyses estimated odds ratios (ORs) and 95% confidence intervals (CIs), primarily comprising indirect comparisons between non-steroidal topicals using a common vehicle comparator.

***Results*:** Twenty-two RCTs (5843 participants) were included. Ruxolitinib demonstrated the highest odds of IGA-TS versus vehicle at week 2 (OR 8.94; 95% CI 5.28–15.12), 4 (OR 9.03; 95% CI 6.27–13.01) and 8 (OR 9.03; 95% CI 6.52–12.50), along with EASI-75 and EASI-90. Difamilast demonstrated favourable EASI-75 (OR 5.34; 95% CI 3.51–8.12) and EASI-90 (OR 6.71; 95% CI 3.79–11.89) responses versus vehicle at week 4; later data were unavailable.

***Conclusions*:** Efficacy profiles varied across novel non-steroidal topical therapies, with ruxolitinib demonstrating the strongest and most consistent relative efficacy estimates. Response magnitude and timing remain important considerations when selecting topical AD treatments.

Keywords: Atopic dermatitis; Difamilast; Eczema; Roflumilast; Ruxolitinib; Tapinarof

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s13555-026-01968-8.

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Published online: 10 November 2026

Key Summary Points

Why carry out this study?

Atopic dermatitis (AD) is a chronic inflammatory skin disease characterized by pruritic, eczematous lesions and psychosocial burden.

This network meta-analysis aimed to compare the efficacy of novel non-steroidal therapies for AD, over the first 8 weeks of treatment, primarily relying on indirect comparisons based on common vehicle comparators.

What was learnt from the study?

Ruxolitinib 1.5% twice daily demonstrated the numerically highest odds of treatment success along with Eczema Area and Severity Index (EASI)-75 and EASI-90 response at weeks 2, 4 and 8. While difamilast 1% twice daily demonstrated favourable EASI-75 and EASI-90 responses against vehicle at week 4, later data were unavailable.

Non-steroidal topical therapies in this analysis demonstrated distinct patterns of response onset and magnitude. Rapid response may represent an important aspect of therapeutic benefit for patients, however, further research regarding patient-reported outcomes are needed.

INTRODUCTION

Atopic dermatitis (AD) is a chronic inflammatory skin disease characterized by pruritus, eczematous lesions and substantial psychosocial burden [1]. Although topical corticosteroids remain the cornerstone of treatment in AD, concerns regarding long-term adverse effects and patient adherence have driven the development of several non-steroidal topical therapies. Recent advances have expanded to include phosphodiesterase-4 (PDE4) inhibitors, Janus kinase (JAK) inhibitors and aryl hydrocarbon receptor (AhR) agonists, each targeting distinct inflammatory pathways involved in AD pathogenesis [2].

As the therapeutic landscape continues to evolve, treatment selection increasingly depends not only on overall efficacy but also the speed with which clinical improvement is achieved. Rapid symptomatic relief may improve quality of life, reduce sleep disturbance and enhance treatment adherence [3, 4]. However, despite the growing number of available non-steroidal topical agents, direct comparative evidence remains limited, and the relative onset of efficacy has not been comprehensively evaluated. In particular, difamilast, a recently approved US Food and Drug Administration (FDA) topical PDE4 inhibitor, has demonstrated promising efficacy in randomized clinical trials, yet its comparative performance relative to other non-steroidal topical therapies remains unclear [5].

Accordingly, this systematic review and network meta-analysis aims to compare the efficacy of novel non-steroidal topical therapies currently available for AD using clinician-reported measures.

METHODS

This analysis was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines. An a priori protocol was registered on PROSPERO (CRD420261452334). This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors; as such, ethical approval was not considered necessary.

Search Strategy and Eligibility Criteria

MEDLINE, Embase, PubMed and Web of Science were searched from inception to July 2026 using keywords related to 'atopic dermatitis' and 'non-steroidal.' A complete search strategy is available in Supplementary Table S1. Reference list searching for any trials not captured originally by the search strategy was also conducted. Randomized controlled trials enrolling patients with AD of any age were included if they evaluated the efficacy of novel non-steroidal therapies. We

defined these as difamilast, tapinarof, ruxolitinib or roflumilast, reflecting their more recent introduction into the AD treatment landscape and emergence as newer non-steroidal treatment options. No restrictions on trial phase or masking status were applied. Approved formulations included difamilast 1% twice daily (BID), tapinarof 1% once daily (QD), ruxolitinib 1.5% BID and roflumilast 0.05% or 0.15% QD. Both roflumilast doses were evaluated as separate nodes to account for potential dose-specific differences in treatment response. Conference abstracts, duplicate results, studies without available English translations and single-arm trials were excluded.

Data Extraction

Using Covidence, retrieved results were independently screened in duplicate by reviewers (S.G., M.B. and L.L.), with discrepancies resolved via consensus. Data were extracted using a standardized form in Microsoft Excel. Outcomes of interest included the proportion of patients achieving treatment success in Investigator's Global Assessment Treatment Success (IGA-TS; score of 0 or 1 with a ≥ 2-point improvement from baseline) or a 50%, 75% or 90% improvement in Eczema Area and Severity Index (EASI) scores at weeks 1, 2, 4 or 8. Where numerical values were unavailable in manuscript text, tables, appendices or associated trial-registry records, data were digitized from published graphs using Automeris.io.

Statistical Analyses

All statistical analyses were conducted using R (version 4.5.1). Frequentist network meta-analyses were performed to determine the comparative efficacy of non-steroidal therapies, reported as odds ratios (ORs) and 95% confidence intervals (CIs). Due to the lack of available head-to-head trials, comparative effects were estimated indirectly using vehicle arms as the common comparator. Random-effects models were used to account for potential heterogeneity across study populations. Continuity corrections were applied when zero events occurred in one arm. Heterogeneity was assessed using the I^2 statistic for each outcome and was considered substantial when exceeding 50%. Forest plots were used to graphically display findings from all pooled outcomes.

Risk of Bias and Certainty of Evidence

Risk of bias was assessed in duplicate using the Cochrane Risk of Bias 2.0 (RoB 2.0) tool [6], with discrepancies resolved via consensus. Certainty of evidence for each outcome was evaluated using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) framework. All included evidence was derived from randomized controlled trials, and therefore initially rated as high certainty [7]. Ratings were downgraded for concerns related to risk of bias, indirectness, inconsistency, imprecision or publication bias, as appropriate.

RESULTS

Of 3185 non-duplicate results screened, 19 studies reporting 22 randomized trials were included (Supplementary Fig. S1). Baseline characteristics are summarized in Table 1, while individual trials are described in Supplementary Table S2. A total of 5843 participants were analysed of whom 53.0% were female (n = 3096/5843). The mean age of the included participants was 24.3 ± 11.7 (range: 3.2–44.3) years. Included participants typically had mild to moderate disease activity [8], with the majority reporting a baseline IGA score of 3 (80.8%, n = 4650/5754). The mean EASI score at baseline was 10.7 ± 2.1. Among 3705 participants assigned to active therapies, tapinarof 1% QD was the most frequently evaluated intervention, accounting for 997 participants (26.9%).

As per Cochrane RoB 2.0, risk of bias was low in 86.4% (n = 19/22) of trials and some concerns in 13.6% (n = 3/22) of trials (Supplementary Fig. S2). Assessment of the transitivity assumption is summarized in Supplementary Table S3. Sex distribution, baseline disease severity and body surface involvement was generally similar across comparisons. While mean age was specifically lower across

Table 1 Clinical and study characteristics of the included studies

Clinical characteristics (*n* = 5843)	***N*** **(%)**
Age (years), mean ± SD	24.33 ± 11.69
Sex	
Female	3096 (53.0)
Male	2747 (47.0)
Race/ethnicity (*n* = 5563)	
White	2741 (49.3)
Black or African American	1007 (18.1)
Asian	1550 (27.9)
Other	265 (4.8)
Baseline IGA (*n* = 5754)	
2	946 (16.4)
3	4650 (80.8)
4	158 (2.7)
Baseline EASI, mean ± SD (*n* = 5616)	10.71 ± 2.08
Baseline BSA, mean ± SD (*n* = 3614)	15.32 ± 4.88
Intervention	
Difamilast [1% BID]	402 (6.9)
Ruxolitinib [1.5% BID]	894 (15.3)
Roflumilast [0.15% QD]	929 (15.9)
Roflumilast [0.05% QD]	483 (8.3)
Tapinarof [1% QD]	997 (17.1)
Vehicle	2138 (36.6)
Study characteristics (*n* = 22)	
Trial phase	
Phase 2	8 (36.4)
Phase 3	14 (63.6)
Study population	
Paediatric only	5 (22.7)
Adult only	3 (13.6)
Mixed-age	14 (63.6)

IGA Investigator's Global Assessment, *EASI* Eczema Area and Severity Index, *BSA* body surface area, *BID* twice daily, *QD* once daily, *SD* standard deviation

roflumilast 0.05% trials, this aligns with its approval for paediatric populations. Table 2 summarizes pooled ORs and 95% CIs, along with heterogeneity statistics by efficacy outcomes. Comparisons between non-steroidal therapies were generally derived from indirect comparisons using a common vehicle comparator, except for one trial directly comparing roflumilast 0.05% and 0.15% (Supplementary Fig. S3). Evidence was generally of moderate-to-high certainty as per GRADE (Supplementary Table S4).

Investigator's Global Assessment Treatment Success

IGA Treatment Success results are summarized in Fig. 1. Compared with vehicle, ruxolitinib 1.5% BID demonstrated the numerically highest odds of achieving IGA-TS among evaluated therapies at week 2 (OR 8.94; 95% CI 5.28–15.12), week 4 (OR 9.03; 95% CI 6.27–13.01) and week 8 (OR 9.03; 95% CI 6.52–12.50). Ruxolitinib data were not available at week 1. At weeks 4 and 8, ruxolitinib 1.5% BID demonstrated significantly

Table 2 Efficacy outcomes are summarized as ORs and 95% CIs from frequentist random-effects network meta-analyses in comparison with vehicle arms

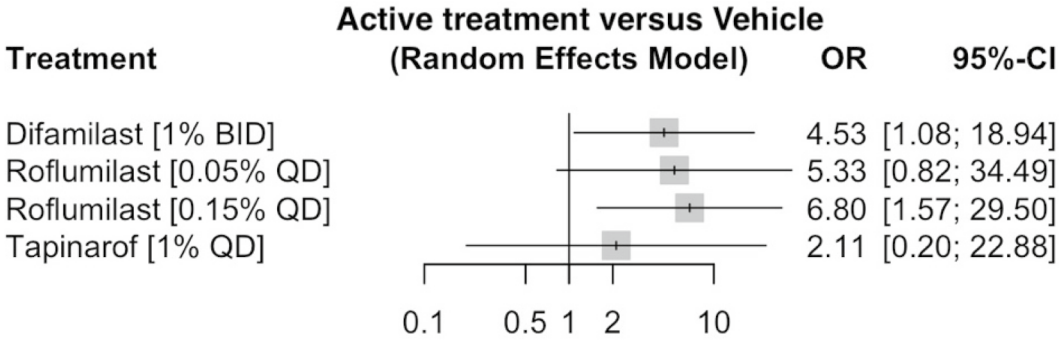
Outcome	OR (95% CI)					I^{2a}
	RUX [1.5% BID]	TAP [1% QD]	DIF [1% BID]	ROF [0.15% QD]	ROF [0.05% QD]	
IGA-TS						
Week 1	NR	2.11 (0.20–22.88)	4.53 (1.08–18.94)	6.80 (1.57–29.50)	5.33 (0.82–34.49)	56.50
Week 2	8.94 (5.28–15.12)	4.01 (1.97–8.18)	4.39 (2.72–7.10)	3.93 (2.65–5.83)	3.01 (1.82–4.99)	0.00
Week 4	9.03 (6.27–13.01)	3.15 (1.95–5.10)	4.22 (2.91–6.14)	2.69 (2.02–3.57)	2.78 (1.84–4.19)	0.00
Week 8	9.03 (6.52–12.50)	4.53 (3.38–6.07)	2.77 (1.35–5.68)	NR	NR	0.00
EASI-50						
Week 2	6.45 (4.55–9.15)	5.19 (2.42–11.14)	NR	NR	NR	0.00
Week 4	7.58 (5.49–10.48)	6.21 (3.39–11.39)	4.22 (2.92–6.09)	NR	NR	0.00
Week 8	6.19 (4.27–8.96)	9.87 (5.30–18.35)	NR	NR	NR	0.00
EASI-75						
Week 2	10.03 (5.93–16.98)	2.44 (1.11–5.34)	NR	2.72 (1.70–4.35)	2.01 (1.08–3.74)	35.00
Week 4	8.05 (5.94–10.91)	3.30 (2.05–5.31)	5.34 (3.51–8.12)	2.72 (2.12–3.48)	2.69 (1.92–3.79)	33.80
Week 8	8.10 (5.56–11.78)	5.12 (3.65–7.18)	NR	NR	NR	37.20
EASI-90						
Week 2	13.77 (5.28–35.94)	1.86 (0.70–4.93)	NR	NR	NR	0.00
Week 4	9.71 (5.81–16.21)	2.57 (1.35–4.86)	6.71 (3.79–11.89)	NR	NR	0.00
Week 8	8.75 (5.57–13.73)	4.11 (2.85–5.93)	NR	NR	NR	8.60

ORs greater than 1 favour the active treatment over vehicle

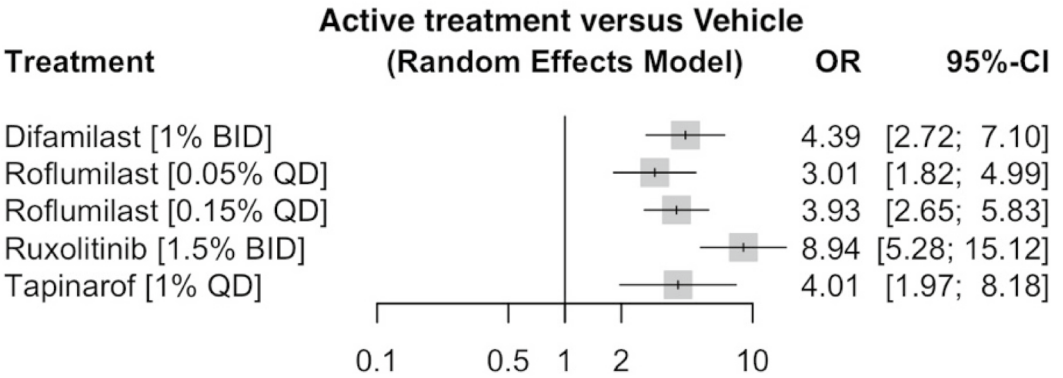
BID twice daily, *CI* confidence interval, *DIF* difamilast, *EASI* Eczema Area and Severity Index, *IGA-TS* Investigator's Global Assessment Treatment Success, *NR* not reported, *OR* odds ratio, *ROF* roflumilast, *RUX* ruxolitinib, *TAP* tapinarof, *QD* once daily

[a] I^2 values represent heterogeneity from complete network comparisons

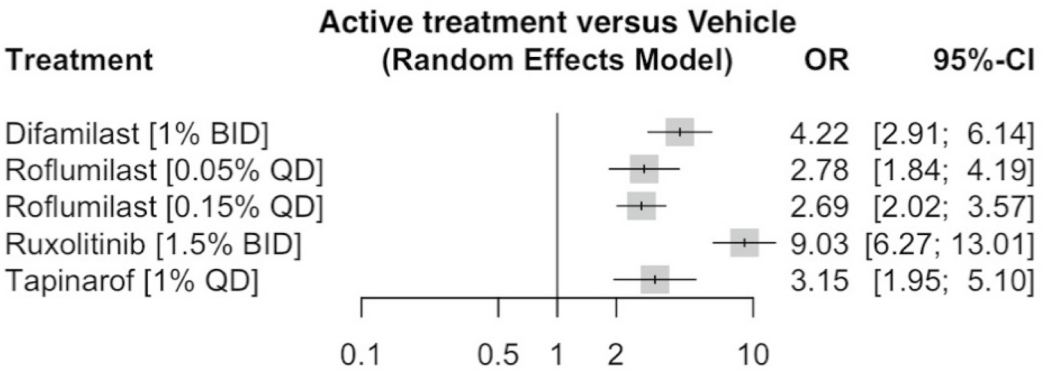
Week 1



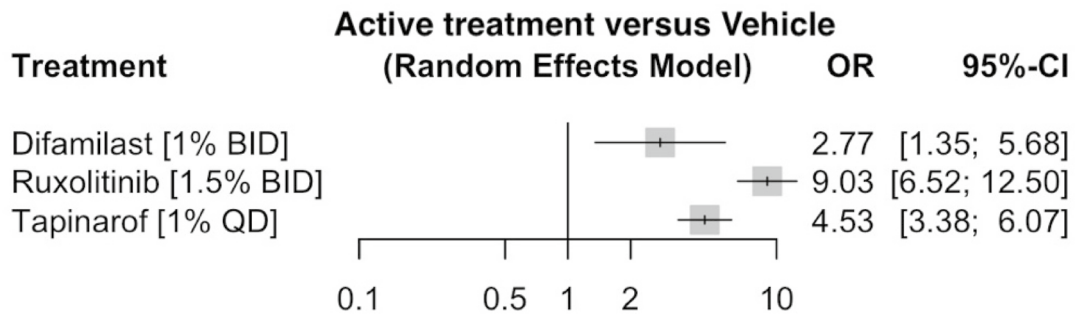
Week 2



Week 4



Week 8



◂**Fig. 1** Forest plots of IGA-TS outcomes at weeks 1, 2, 4 and 8 in non-steroidal therapies compared with vehicle arms from frequentist random-effects network meta-analysis. Reported as ORs and 95% CIs, where ORs greater than 1 favour the active treatment. *BID* twice daily, *CI* confidence interval, *IGA-TS* Investigator's Global Assessment Treatment Success, *OR* odds ratio, *QD* once daily

higher estimated odds of achieving IGA-TS than the other evaluated non-steroidal therapies in indirect comparisons, whereas at week 2, not all comparisons reached statistical significance.

Tapinarof 1% QD (OR 2.11; 95% CI 0.20–22.88) did not achieve statistical significance in treatment success compared with vehicle at week 1. However, response rates in tapinarof users gradually improved over the assessed time points, reaching its highest observed effect versus vehicle at week 8 (OR 4.53; 95% CI 3.38–6.07). Difamilast 1% BID demonstrated statistically significant improvements in treatment success versus vehicle at weeks 2, 4 and 8. The estimated effect was numerically lower at week 8 (OR 2.77; 95% CI 1.35–5.68) than at week 1 (OR 4.53; 95% CI 1.08–18.94); however, estimates were derived from separate time-specific analyses and had overlapping confidence intervals. Roflumilast demonstrated similar reductions in IGA-TS response at both dosages from week 1 (0.15% QD: OR 6.80; 0.05% QD: OR 5.33) to week 4 (0.15% QD: OR 2.69; 0.05% QD: OR 2.78).

Eczema Area and Severity Index

EASI outcomes were available beginning at week 2, although difamilast contributed EASI data only from week 4 onwards across all response thresholds.

EASI-50 analyses were limited to ruxolitinib, tapinarof and difamilast (Supplementary Fig. S4). At week 2, ruxolitinib 1.5% BID demonstrated the numerically highest odds of achieving EASI-50 versus vehicle (OR 6.45; 95% CI 4.55–9.15), with tapinarof 1% QD demonstrating slightly lower odds (OR 5.19; 95% CI 2.42–11.14). Ruxolitinib 1.5% BID maintained the highest estimated response compared with vehicle at week 4 (OR 7.58; 95% CI 5.49–10.48), followed by tapinarof 1% QD (OR 6.21; 95% CI 3.39–11.39) and difamilast 1% BID (OR 4.22; 95% CI 2.92–6.09). However, the magnitude of benefit relative to individual active comparators varied across indirect comparisons, and statistically significant superiority was not consistently demonstrated for EASI-50.

Figure 2 displays EASI-75 response rates across non-steroidal therapies. All assessed formulations achieved statistically significant EASI-75 responses compared with vehicle at week 2, led by ruxolitinib 1.5% BID (OR 10.03; 95% CI 5.93–16.98). Ruxolitinib maintained the strongest effect size at week 4 (OR 8.05; 95% CI 5.94–10.91). Difamilast 1% BID was almost five times more likely to achieve EASI-75 compared with vehicle (OR 5.34; 95% CI 3.51–8.12), while tapinarof 1% QD was almost three times more likely (OR 3.30; 95% CI 2.05–5.31). Roflumilast 0.05% QD consistently demonstrated the lowest odds of achieving EASI-75 across all evaluated therapies, with slight improvement from week 2 (OR 2.01; 95% CI 1.08–3.74) to week 4 (OR 2.69; 95% CI 1.92–3.79). Of the two therapies with available EASI-75 data for week 8, ruxolitinib 1.5% BID retained significantly elevated response rates relative to vehicle (OR 8.10; 95% CI 5.56–11.78). Tapinarof 1% QD improved at week 8, with approximately five-fold higher odds of EASI-75 response versus vehicle (OR 5.12; 95% CI 3.65–7.18).

EASI-90 analyses were limited to ruxolitinib, tapinarof and difamilast (Fig. 3). At week 2, ruxolitinib 1.5% BID was significantly more likely to achieve EASI-90 versus vehicle (OR 13.77; 95% CI 5.28–35.94), whereas tapinarof 1% QD did not reach statistical significance (OR 1.86; 95% CI 0.70–4.93). Ruxolitinib continued to demonstrate the highest odds of achieving EASI-90 response across evaluated therapies at week 4 (OR 9.71; 95% CI 5.81–16.21) and week 8 (OR 8.75; 95% CI 5.57–13.73). Difamilast 1% BID contributed EASI-90 data at week 4, showing substantial efficacy versus vehicle (OR 6.71; 95% CI 3.79–11.89), followed by tapinarof 1% QD (OR 2.57; 95% CI 1.35–4.86). Tapinarof efficacy increased over time, with an almost two-fold improvement in odds of achieving EASI-90 from

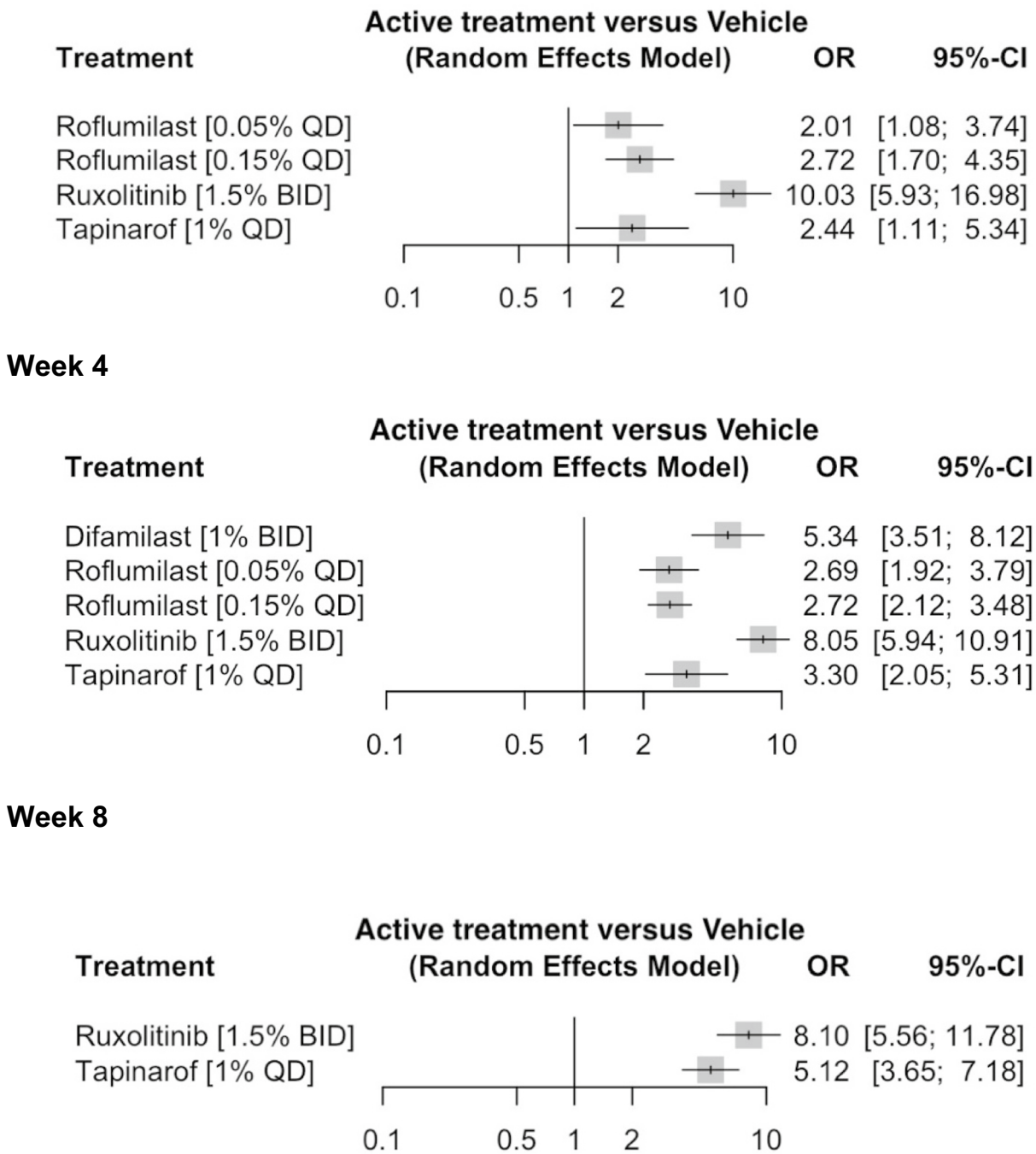


Fig. 2 Forest plots of EASI-75 outcomes at weeks 2, 4 and 8 in non-steroidal therapies compared with vehicle arms from frequentist random-effects network meta-analysis. Reported as ORs and 95% CIs, where ORs greater than 1 favour the active treatment. *EASI* Eczema Area and Severity Index, *BID* twice daily, *CI* confidence interval, *OR* odds ratio, *QD* once daily

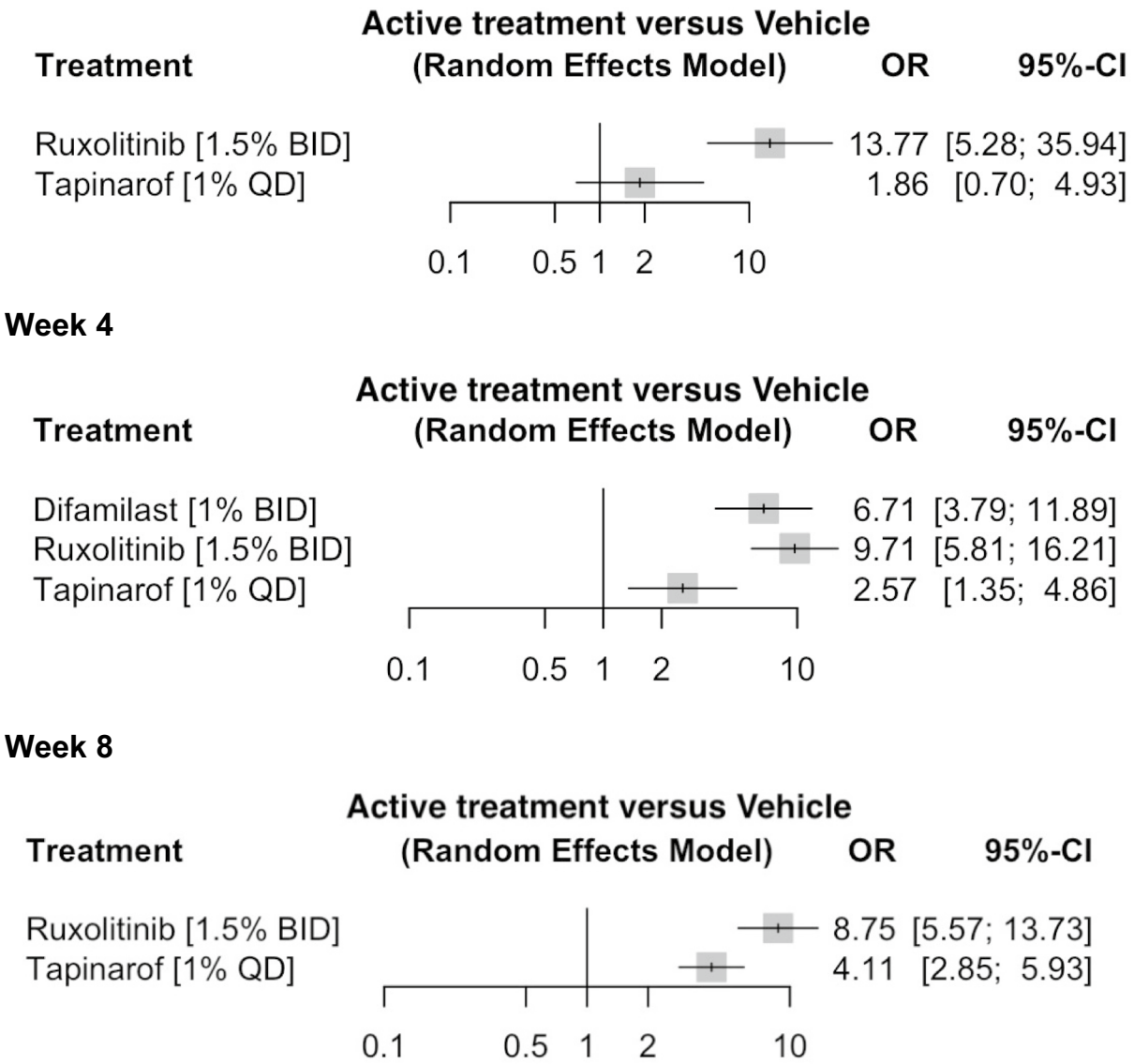


Fig. 3 Forest plots of EASI-90 outcomes at weeks 2, 4 and 8 in non-steroidal therapies compared with vehicle arms from frequentist random-effects network meta-analysis. Reported as ORs and 95% CIs, where ORs greater than 1 favour the active treatment. *EASI* Eczema Area and Severity Index, *BID* twice daily, *CI* confidence interval, *OR* odds ratio, *QD* once daily

week 2 to week 8 (OR 4.11; 95% CI 2.85–5.93). EASI-90 data were not available for roflumilast 0.15% QD or 0.05% QD at any assessed time point.

DISCUSSION

This network meta-analysis evaluated the comparative onset of efficacy of non-steroidal topical therapies across 5843 patients with AD over the first 8 weeks of treatment, with generally

high certainty of evidence. Overall, ruxolitinib 1.5% BID demonstrated the most consistent comparative efficacy against a common vehicle comparator across clinician-reported outcomes, generally achieving the highest point estimates of IGA-TS and EASI responses at weeks 2, 4 and 8. However, these estimates should not be interpreted as evidence of statistical superiority over other non-steroidal therapies in the absence of direct head-to-head comparisons. Additionally, treatment effects varied over time, with tapinarof 1% QD demonstrating increasing efficacy at later assessments, particularly for EASI outcomes. When available, difamilast 1% BID generally had the second-largest point estimate among treatments evaluated, with substantial response against vehicle at higher EASI thresholds. Despite strong early efficacy in IGA-TS, roflumilast demonstrated comparatively weaker effects at later time points and in EASI response, at both adult-approved (0.15% QD) and paediatric-approved (0.05% QD) dosages. Collectively, these findings highlight that differences in therapeutic profiles may extend beyond overall efficacy, with timing of clinical response posing important considerations among available non-steroidal topical therapies.

Although the exact contributing mechanisms remain unclear, the rapid onset of action observed with ruxolitinib is consistent with its classification as a selective JAK1/JAK2 inhibitor [9]. The JAK-STAT pathway represents a key signaling pathway in AD pathogenesis, with inhibition leading to downstream suppression of cytokines including interleukin (IL)-4, IL-13 and IL-31 signaling [10]. This mechanism of action could contribute to the simultaneous suppression of multiple inflammatory pathways involved in type 2 inflammation, pruritus and epidermal barrier dysfunction [11], possibly explaining its substantial improvement over vehicle comparators. From a clinical standpoint, this rapid response may be particularly relevant for patients experiencing substantial pruritus, sleep disruption or psychosocial burden, with early disease control possibly improving treatment satisfaction and adherence [3, 12].

Although ruxolitinib demonstrated the most robust response, our findings indicate variations in therapeutic trajectories among non-steroidal topical agents. Tapinarof demonstrated progressively increasing efficacy across all EASI response thresholds. This pattern may reflect the wide-ranging effects of AhR agonism. Activation of AhR by tapinarof has been shown to promote epidermal differentiation and barrier restoration, while also reducing inflammatory signaling through effects on T helper (Th) 17/Th22 pathways and downstream cytokine production [13, 14]. Unlike therapies that primarily suppress inflammatory signaling, AhR agonism may involve broader changes in both immune regulation and epidermal normalization, which may require additional time to manifest clinically. This profile may potentially explain the gradual accumulation of clinical benefit observed over subsequent weeks; however, further research is required to confirm these proposed mechanisms. PDE4 inhibitors in this review demonstrated comparable responses relative to vehicle. At week 4, difamilast demonstrated relatively favourable efficacy estimates, particularly for EASI-75 and EASI-90 responses. However, data at later time points were not available, restricting assessment of longer-term efficacy trajectories compared with other agents. Although the precise mechanism remains unclear, the broad anti-inflammatory effects of PDE4 inhibition may contribute to the clinical improvements observed in AD [15, 16]. Differences between individual PDE4 inhibitors may reflect variations in molecular selectivity, pharmacokinetic properties and trial populations. Pre-clinical studies suggest that difamilast may preferentially inhibit PDE4B; however, the clinical relevance of this property and its comparative implications remain uncertain [17]. It also remains unclear whether the weaker apparent effects of roflumilast reflect lower intrinsic efficacy of the active molecule or, alternatively, a stronger therapeutic contribution from the vehicle formulation itself, which may provide barrier-repair and emollient effects that improve clinical outcomes independent of PDE4 inhibition [18, 19].

While efficacy is commonly considered at traditional trial endpoints, specifically at week 8 or later, speed of therapeutic response increasingly represents an important consideration in treatment selection. Patients with significant disease-related burden may prioritize rapid

improvement and thus derive greater benefit from agents demonstrating early separation from vehicle, whereas therapies with increasing efficacy over time may remain valuable options for sustained disease control. Rapid improvement of AD may additionally encourage continued use, especially as topical therapies can be labour-intensive and require frequent application [3, 20]. Treatment choice should therefore incorporate individual patient priorities, accessibility and affordability, disease severity, affected body sites, safety and expectations regarding the timing of improvement.

Several limitations should be considered in the interpretation of this analysis. First, the absence of direct head-to-head trials between active therapies necessitated reliance on indirect comparisons. Although these meta-analyses may enable comparative estimation across multiple interventions that have not been directly compared, differences in unreported population demographics, trial characteristics and study design may influence observed associations. Second, the availability of early efficacy data varied substantially across therapies, limiting comprehensive comparisons for certain outcomes and leading to potential instability in effect sizes. In particular, difamilast primarily contributed week 4 data whereas EASI data were lacking for roflumilast trials, resulting in small network sizes and limited assessment of response patterns. Exclusion of non-English-language studies and conference abstracts may have resulted in omission of potentially relevant data, while also introducing possible language bias. Third, age-stratified data were not consistently reported across the included studies, limiting subgroup assessments of responses in formulations specifically approved for adult versus paediatric populations in this review. Furthermore, patient-reported outcomes could not be reasonably assessed in this review due to heterogeneity across trials and limited data availability.

CONCLUSIONS

This network meta-analysis demonstrates that non-steroidal topical therapies for AD exhibit distinct patterns of onset and magnitude of clinical response. Ruxolitinib 1.5% BID demonstrated the most consistent efficacy across IGA and EASI outcomes versus vehicle controls across the first 8 weeks, whereas tapinarof 1% QD showed increasing relative efficacy with continued treatment. Difamilast 1% BID also demonstrated favourable efficacy, particularly at higher EASI thresholds, although longer-term data remain limited. Both the timing and magnitude of response represent important considerations when selecting non-steroidal topical therapies and may guide individualized treatment decisions in AD based on patient priorities. Further head-to-head trials incorporating patient-reported outcomes as well as stratification by age, baseline severity and other relevant effect modifiers may provide additional insight into the benefit of early symptomatic relief in AD.

ACKNOWLEDGEMENTS

We thank all trial participants represented in this analysis, along with the trial investigators for their contributions in generating the data used in this manuscript.

Author Contributions. All authors have approved and reviewed the final manuscript in line with ICMJE guidelines. Conceptualization: Mohannad Abu-Hilal, Sana Gupta. Investigation: Sana Gupta, Madison Bell, Laurel Liu. Formal analysis: Sana Gupta. Writing—original draft: Sana Gupta, Grace Xiong, Madison Bell, Laurel Liu. Writing—reviewing and editing: Sana Gupta, Grace Xiong, Mohannad Abu-Hilal.

Funding. No funding or sponsorship was received for this study or publication of this article. The Rapid Service Fee was funded by the authors.

Data Availability. All data generated or analyzed during this study are included in this published article as supplementary information files.

Declarations

Conflict of Interest. Sana Gupta, Madison Bell, Laurel Liu, Grace Xiong and Mohannad Abu-Hilal have nothing to disclose.

Ethical Approval. This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

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