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Comparative Efficacy of Biologics in Combination With Topical Corticosteroids for Treatment of Moderate to Severe Atopic Dermatitis: A Systematic Review and Bayesian Network Meta-Analysis

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ABSTRACT

BACKGROUND: We compared the efficacy and safety of the biologics dupilumab, lebrikizumab, tralokinumab and nemolizumab administered with background topical corticosteroids (TCS) in moderate to severe atopic dermatitis.

METHODS: We performed a systematic review and Bayesian random-effects network meta-analysis of phase 3, placebo-controlled randomized clinical trials (RCTs) evaluating dupilumab 300 mg once weekly (QW), dupilumab 300 mg every two weeks (Q2W), lebrikizumab 250 mg Q2W, tralokinumab 300 mg Q2W, and nemolizumab 30 mg Q4W, each administered with

background TCS. The Eczema Area and Severity Index (EASI-75), EASI-90, Investigator's Global Assessment (IGA) 0/1, Peak Pruritus Numerical Rating Scale (PP-NRS4), surface under the cumulative ranking curve (SUCRA) at Week 16 and descriptive safety outcomes were compared.

RESULTS: Across five RCTs (N = 3,059), compared with placebo, dupilumab 300 mg demonstrated the highest likelihood of achieving EASI-75 (Q2W: OR 7.46, 95% CrI 1.21–45.45; QW: OR 5.90, 95% CrI 0.94–34.83), followed by lebrikizumab (OR 3.20, 95% CrI 0.49–20.18), tralokinumab (OR 2.29, 95% CrI 0.39–13.16), and nemolizumab (OR 1.79, 95% CrI 0.50–6.53). For EASI-90 and IGA 0/1, dupilumab 300 mg QW ranked highest, followed by dupilumab 300 mg Q2W (the indicated dose), lebrikizumab, tralokinumab, and nemolizumab. For itch reduction, dupilumab 300 mg QW ranked highest, followed by dupilumab 300 mg Q2W, nemolizumab, lebrikizumab, and tralokinumab. SUCRA rankings consistently favored dupilumab across objective skin-clearance outcomes. All biologics demonstrated acceptable safety profiles.

CONCLUSIONS: Dupilumab demonstrated the most consistent short-term efficacy, providing superior skin clearance and itch reduction. Lebrikizumab, tralokinumab, and nemolizumab showed intermediate benefits.

KEYWORDS: Atopic dermatitis; Bayesian network meta-analysis; Biologic therapy; Combination therapy; Dupilumab; Lebrikizumab; Nemolizumab; Tralokinumab; Topical corticosteroids; Eczema Area and Severity Index

INTRODUCTION

Atopic dermatitis (AD) is a chronic, relapsing inflammatory skin disease characterized by eczematous lesions, persistent pruritus, and sleep disturbance, each of which contributes to substantial physical, psychological, and social impairment [1-3]. Pruritus is the hallmark and most burdensome symptom of AD, frequently intensifying at night and leading to sleep disruption, daytime fatigue, and diminished health related quality of life [4, 5]. AD imposes considerable psychosocial and socioeconomic burdens on patients and caregivers, especially those with moderate to severe disease who frequently have inadequate control with topical therapy alone and recurrent flares necessitating systemic treatment [6, 7]. Prior to the introduction of targeted

biologics, management of refractory AD relied heavily on high potency topical corticosteroids (TCS), systemic corticosteroids, and conventional immunosuppressants, approaches supported by limited evidence and constrained by long term safety concerns.

Although TCS and topical calcineurin inhibitors (TCIs) remain foundational treatments for mild disease, a substantial proportion of patients with moderate-to-severe AD fail to achieve adequate disease control with topical therapy alone and therefore require systemic treatment. Over the past decade, advances in the understanding of AD immunopathogenesis have led to the development of targeted biologic therapies that selectively inhibit key cytokine pathways involved in disease progression [8, 9]. These biologics have transformed the treatment landscape by providing effective disease control with favorable long-term safety profiles.

Currently, four biologic agents are approved for the treatment of moderate-to-severe AD. Dupilumab, tralokinumab, and lebrikizumab are approved for moderate to severe AD as monotherapy and in combination with TCS, whereas nemolizumab is approved only for use in combination with TCS. Dupilumab is a fully human monoclonal antibody that binds the IL-4 receptor α (IL-4Rα), thereby inhibiting signaling of both IL-4 and IL-13, the principal cytokines driving type 2 inflammation [10]. Although dupilumab is highly effective, a substantial proportion of patients still fail to reach stringent endpoints such as Eczema Area and Severity Index 90% improvement (EASI 90) or Investigator's Global Assessment for AD (0/1) (IGA 0/1) during the induction phase. This therapeutic gap has driven interest in developing high affinity IL 13–targeting biologics designed to achieve deeper skin clearance. Tralokinumab is a fully human monoclonal antibody that selectively neutralizes IL-13, preventing its interaction with IL-13 receptor α1 and α2 [11]. Lebrikizumab is a high-affinity monoclonal antibody against IL-13 that binds a distinct epitope, preventing IL-13 signaling through the IL-4Rα/IL-13Rα1 receptor complex while preserving IL-13 binding to the decoy receptor IL-13Rα2 [12]. Nemolizumab, an IL-31Rα antagonist, is the most recently introduced biologic, although Phase 3 clinical trials evaluated it only in combination with low and/or medium potency TCS and/or TCI [13]. Owing to these distinct mechanisms of action, differences in efficacy across skin clearance and itch outcomes may be expected.

Dupilumab, lebrikizumab, tralokinumab, and nemolizumab are all approved by the U.S. FDA for moderate-to-severe AD, with nemolizumab indicated only in combination with TCS. In the E.U., all four agents are authorized by the EMA for moderate-to-severe AD without this restriction. In Japan, dupilumab, lebrikizumab, and tralokinumab are approved for AD in patients with inadequate response to existing therapies, whereas nemolizumab is indicated specifically for pruritus in patients with AD whose itch remains uncontrolled despite appropriate topical anti-inflammatory and anti-allergic treatment. Among these biologics, only dupilumab is currently approved by the NMPA in China for moderate-to-severe AD.

Despite the availability of multiple biologic therapies, direct head to head randomized controlled trials (RCTs) comparing these agents are limited, in part because non inferiority designs require large sample sizes to detect modest differences among already effective treatments. Consequently, treatment selection often relies on indirect comparisons across separate placebo controlled studies. Because AD trials commonly use placebo comparators, network meta analysis offers a practical framework for cross trial comparisons anchored to a shared control group and can generate provisional efficacy and safety rankings. However, previous network meta analyses have frequently combined biologics with Janus kinase (JAK) inhibitors, included investigational agents, previously abandoned dosing regimens, pooled monotherapy and combination therapy studies, or evaluated outcomes at different follow up time points, thereby increasing clinical heterogeneity and limiting the applicability of their findings to contemporary practice.

To address these gaps, we conducted a systematic review and Bayesian network meta-analysis of phase 3 RCTs evaluating currently approved biologic therapies administered in combination with background TCS and/or TCIs in adolescents and/or adults with moderate-to-severe AD. We compared the relative efficacy of dupilumab, tralokinumab, lebrikizumab, and nemolizumab using clinically relevant outcomes at Week 16, including EASI-75, EASI-90, IGA, and Peak Pruritus Numerical Rating Scale (PP-NRS) response. Additionally, we performed indirect treatment comparisons, estimated treatment rankings using the surface under the cumulative ranking curve (SUCRA), calculated response rates, and summarized available safety data to provide clinically relevant comparative evidence for biologic selection.

METHODS

Protocol and Reporting Guidelines

This systematic review and Bayesian network meta-analysis (BNMA) was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement and the PRISMA extension for Network Meta-Analyses (PRISMA-NMA) [14], using an a priori protocol registered in PROSPERO (REDACTED).

Eligibility Criteria

RCTs evaluating targeted systemic therapies administered in combination with background topical therapy for patients with moderate-to-severe AD were considered eligible. Phase 3 trials enrolling adolescent and/or adult patients were included. Eligible studies compared an active intervention plus TCS and/or TCIs with placebo plus the corresponding background topical therapy and reported at least one predefined efficacy outcome at Week 16.

Studies evaluating monotherapy, non-randomized studies, observational studies, conference abstracts without sufficient data, duplicate publications, animal studies, and studies not published in English were excluded.

Literature Search

A comprehensive literature search was conducted in PubMed/MEDLINE, Embase, the Cochrane Central Register of Controlled Trials (CENTRAL), and ClinicalTrials.gov from database inception to the final search date. Search terms included combinations of controlled vocabulary and free-text keywords related to "atopic dermatitis," "eczema," "dupilumab," "tralokinumab," "nemolizumab," "lebrikizumab," "biologic therapy," "randomized controlled trial," and related synonyms.

Study Selection

Following removal of duplicate records, two reviewers independently screened titles and abstracts for eligibility. Full-text articles were subsequently assessed against the predefined inclusion and exclusion criteria. Disagreements were resolved through discussion until consensus was reached.

Data Extraction

Two reviewers independently extracted data using a standardized data extraction form. Extracted variables included study characteristics (author, publication year, trial name, study phase, registration number, country, study design, treatment duration, intervention, comparator, background topical therapy, and sample size), participant characteristics (age, sex, disease duration, baseline EASI, IGA, and PP-NRS), intervention details (dose, frequency, route of administration, and treatment duration), and efficacy and safety outcomes.

Interventions

The treatment network included dupilumab 300 mg once weekly (QW), an unapproved dosing regimen plus TCS following a 600 mg loading dose [15], dupilumab 300 mg every two weeks (Q2W), the approved dosing regimen plus TCS following a 600 mg loading dose [15], tralokinumab 300 mg (Q2W) plus TCS following a 600 mg loading dose, nemolizumab 30 mg every four weeks (Q4W) plus TCS with or without TCIs following a 60 mg loading dose [16], and lebrikizumab 250 mg Q2W plus TCS [17] following 500 mg loading dose at baseline and Week 2. Placebo administered with the corresponding background topical therapy served as the common comparator. Each treatment regimen was considered a separate intervention node within the Bayesian treatment network.

Outcomes

All efficacy and safety outcomes were assessed at Week 16. The primary outcome was the proportion of patients achieving an EASI-75. Secondary efficacy outcomes included the proportions of patients achieving EASI-90, an IGA score of 0 or 1, with a ≥ 2-point improvement from baseline, and a ≥4-point improvement from baseline in the PP-NRS4. Safety outcomes included the incidence of any adverse event (AE), serious adverse events (SAEs), serious infections, discontinuation due to adverse events, conjunctivitis, herpes infection, and death.

Risk of Bias Assessment

The methodological quality of the included studies was independently assessed by two reviewers using the Cochrane Risk of Bias 2 (RoB 2) tool [18]. The following domains were evaluated: bias arising from the randomization process, bias due to deviations from intended interventions, bias due to missing outcome data, bias in outcome measurement, and bias in selection of the reported

results. Each study was classified as having a low risk of bias, some concerns, or a high risk of bias. Disagreements were resolved through discussion.

Statistical Analysis

Separate Bayesian network meta-analyses were performed for each efficacy outcome. Because definitions and reporting methods for adverse events varied across trials, safety outcomes were summarized descriptively. Treatment effects were estimated as odds ratios (ORs) with corresponding 95% credible intervals (CrIs).

A Bayesian random-effects model with a binomial likelihood and logit link function was used to account for between-study heterogeneity. Posterior estimates were generated using Markov chain Monte Carlo (MCMC) simulation. Model convergence was evaluated by visual inspection of trace plots and the Brooks–Gelman–Rubin diagnostic.

Network geometry was illustrated using a network plot in which nodes represent treatment interventions and edges represent direct treatment comparisons. Treatment ranking probabilities were estimated from the posterior distributions to determine the relative efficacy and safety of the included interventions.

The transitivity assumption was assessed by comparing important clinical and methodological characteristics across studies, including participant demographics, baseline disease severity, treatment duration, study design, and background topical therapy. Consistency between direct and indirect evidence was planned to be evaluated using node-splitting analyses where closed loops were available. However, because the final treatment network contained no closed loops, formal consistency assessment was not feasible. Absolute response probabilities were estimated by applying the posterior relative treatment effects to a common placebo baseline risk.

All statistical analyses were performed using R statistical software (version 4.5.1; R Foundation for Statistical Computing, Vienna, Austria) [19]. Bayesian network meta-analysis was conducted using the gemtc, rjags, and coda packages.

RESULTS

Study Characteristics

A total of 1,120 records were identified through database and clinical trial registry searches, including 344 from PubMed, 104 from Embase, 654 from the Cochrane Library, and 18 from ClinicalTrials.gov. After removing 466 duplicate records, 654 unique records remained for title and abstract screening. Of these, 508 records were excluded, and 146 full-text reports were sought for retrieval. Following full-text review, 141 reports were excluded because they were non-randomized studies, evaluated non-AD dermatologic conditions, lacked a placebo comparator, or were conference abstracts, posters, or study protocols. Ultimately, five phase 3 RCTs [15, 16, 20, 21] met the inclusion criteria and were included in the Bayesian network meta-analysis, comprising one trial each evaluating dupilumab, lebrikizumab, tralokinumab, and nemolizumab (Figure 1).

Five phase 3, double-blind, placebo-controlled RCTs involving 3,059 participants were included in the Bayesian network meta-analysis. These studies evaluated dupilumab 300 mg QW [15], dupilumab 300 mg Q2W [15], lebrikizumab 250 mg Q2W [20], tralokinumab 300 mg Q2W [21], and nemolizumab 30 mg Q4W [16], each administered with TCS with or without TCI and preceded by one or more loading doses, compared with placebo plus topical therapy. Trial duration for primary analysis was 16 weeks. Studies were multinational and conducted across North America, Europe, Asia, and Oceania. Four studies evaluated a single biologic regimen, whereas the LIBERTY AD CHRONOS trial evaluated both approved dupilumab dosing regimens [15]. Detailed study characteristics are summarized in Table 1.

Baseline Characteristics

Baseline demographic and disease characteristics were generally balanced across treatment groups. Mean participant age ranged from approximately 33 to 40 years, while the proportion of female participants varied from 34% to 51%. Baseline EASI scores ranged from 27 to 31, indicating moderate-to-severe AD across all studies. Mean baseline PP-NRS4 scores ranged between 7.2 and 7.9, reflecting substantial itch severity. Body surface area involvement was generally between 44% and 59%, and the distribution of baseline IGA scores was comparable across treatment groups. Overall, the included populations were clinically homogeneous. No major differences were observed in participant age, baseline disease severity (EASI, IGA, PP-NRS, and

BSA), study design, treatment duration, or background topical therapy, supporting the transitivity assumption required for network meta-analysis (Table 2).

Network Geometry and Model Convergence

The Bayesian network meta-analysis included five active biologic regimens (dupilumab 300 mg QW, dupilumab 300 mg Q2W, lebrikizumab 250 mg Q2W, tralokinumab 300 mg Q2W, and nemolizumab 30 mg Q4W) [15, 16, 20, 21], each administered with TCS with or without TCI, and placebo plus the corresponding topical therapy as the common comparator. The treatment network was well connected through the placebo node, allowing estimation of both direct and indirect treatment effects (Figure 2).

Bayesian Network Meta-analysis

EASI-75 Response

Compared with placebo, all biologics demonstrated higher estimated odds of achieving an EASI-75 response at week 16. Dupilumab 300 mg Q2W showed the largest treatment effect (OR 7.46, 95% CrI 1.21–45.45), followed by dupilumab 300 mg QW (OR 5.90, 95% CrI 0.94–34.83) [15]. Lebrikizumab 250 mg Q2W (OR 3.20, 95% CrI 0.49–20.18) [20], tralokinumab 300 mg Q2W (OR 2.29 [21], 95% CrI 0.39–13.16), and nemolizumab 30 mg Q4W (OR 1.79, 95% CrI 0.50–6.53) [16] also favored active treatment over placebo, although their CrIs included the null value (Figure 3).

EASI-90 Response

For EASI-90, dupilumab 300 mg QW demonstrated the highest efficacy versus placebo (OR 6.10, 95% CrI 1.11–33.07), followed by dupilumab 300 mg Q2W (OR 5.30, 95% CrI 0.94–28.18) [15]. Lebrikizumab 250 mg Q2W (OR 2.67, 95% CrI 0.45–15.58), tralokinumab 300 mg Q2W (OR 1.82, 95% CrI 0.32–10.53), and nemolizumab 30 mg Q4W (OR 1.61, 95% CrI 0.49–5.51) were associated with numerically higher odds of achieving EASI-90 than placebo, although these differences were not statistically credible (Figure 4).

IGA 0/1 Response

Dupilumab 300 mg QW achieved the greatest odds of attaining an IGA score of 0/1 compared with placebo (OR 4.56, 95% CrI 1.13–18.90), closely followed by dupilumab 300 mg Q2W (OR 4.46, 95% CrI 1.05–18.71). Lebrikizumab 250 mg Q2W (OR 2.45, 95% CrI 0.57–10.70), tralokinumab 300 mg Q2W (OR 1.81, 95% CrI 0.41–7.52), and nemolizumab 30 mg Q4W (OR 1.71, 95% CrI 0.63–4.51) also demonstrated favorable treatment effects compared with placebo, although their CrIs crossed unity (Figure 5).

PP-NRS4 Response

For improvement in pruritus, dupilumab 300 mg QW showed the highest odds of achieving a PP-NRS4 response versus placebo (OR 5.87, 95% CrI 1.08–30.46), followed by dupilumab 300 mg Q2W (OR 4.26, 95% CrI 0.80–22.05). Nemolizumab 30 mg Q4W also demonstrated statistically credible improvement versus placebo (OR 3.32, 95% CrI 1.07–10.79). Lebrikizumab 250 mg Q2W (OR 2.26, 95% CrI 0.41–12.15) and tralokinumab 300 mg Q2W (OR 1.62, 95% CrI 0.30–8.55) numerically favored active treatment. However, the 95% CrIs for dupilumab Q2W, lebrikizumab, and tralokinumab included unity; therefore, these effects were not statistically credible (Figure 6).

Pairwise Indirect Comparisons

Pairwise indirect comparisons between active biologics revealed no statistically credible differences, as all 95% CrIs included unity. Dupilumab 300 mg Q2W showed numerically higher estimated odds of response than dupilumab 300 mg QW (OR 1.26, 95% CrI 0.21–7.83), lebrikizumab 250 mg Q2W (OR 2.33, 95% CrI 0.17–33.33), tralokinumab 300 mg Q2W (OR 3.23, 95% CrI 0.29–50.00), and nemolizumab 30 mg Q4W (OR 4.17, 95% CrI 0.48–33.33). Lebrikizumab also showed numerically higher estimated efficacy than tralokinumab (OR 1.39, 95% CrI 0.11–19.18) and nemolizumab (OR 1.78, 95% CrI 0.19–16.61). Nemolizumab showed numerically lower estimated efficacy than tralokinumab, although the treatments had broadly comparable effects (OR 0.78, 95% CrI 0.09–7.20) (Figure 7). Overall, dupilumab regimens generally showed numerically greater estimated treatment effects than the other biologics; however, the wide CrIs indicated substantial uncertainty, and no indirect comparison provided statistically credible evidence of superiority.

Treatment Ranking (SUCRA)

Treatment ranking based on SUCRA values placed the dupilumab regimens in the top two positions across all efficacy outcomes (Figure 8). For EASI-75, dupilumab 300 mg Q2W ranked first (SUCRA 87.6%), followed by dupilumab 300 mg QW (77.9%), lebrikizumab 250 mg Q2W (55.4%), tralokinumab 300 mg Q2W (42.2%), nemolizumab 30 mg Q4W (31.0%), and placebo (5.9%). For EASI-90, dupilumab 300 mg QW ranked first (86.1%), followed by dupilumab 300 mg Q2W (79.3%), lebrikizumab Q2W (55.1%), tralokinumab Q2W (39.0%), nemolizumab Q4W (32.9%), and placebo (7.6%). For IGA 0/1, dupilumab 300 mg QW (83.2%) and Q2W (81.3%) occupied the top two positions, followed by lebrikizumab Q2W (54.4%), tralokinumab Q2W (39.1%), nemolizumab Q4W (35.7%), and placebo (6.3%). For PP-NRS4, dupilumab 300 mg QW ranked first (87.4%), followed by dupilumab 300 mg Q2W (71.9%), nemolizumab Q4W (60.9%), lebrikizumab Q2W (43.5%), tralokinumab Q2W (29.4%), and placebo (6.9%). Nemolizumab's comparatively higher ranking for PP-NRS4 suggests a potentially greater effect on itch than on the other assessed efficacy outcomes. However, SUCRA rankings should be interpreted alongside the effect estimates and their uncertainty and do not, by themselves, establish statistically credible superiority between treatments.

Observed Response Rates at Week 16

Responder data from the individual trials contributed additional resolution to the comparative efficacy profile at Week 16. Observed response rates reflect the absolute proportions of responders in each biologic plus background topical therapy arm compared with the corresponding placebo plus background therapy arms. Observed response rates at Week 16 across the included trial arms are shown in Figure 9.

For EASI-75, response rates were highest with dupilumab 300 mg Q2W (45.7%), followed closely by dupilumab 300 mg QW (40.7%). Lebrikizumab 250 mg Q2W achieved a response rate of 27.2%, followed by tralokinumab 300 mg Q2W (20.2%) and nemolizumab 30 mg Q4W (13.3%).

For EASI-90, dupilumab 300 mg QW demonstrated the highest response rate (32.2%), followed by dupilumab 300 mg Q2W (28.5%), lebrikizumab 250 mg Q2W (20.2%), tralokinumab 300 mg Q2W (11.5%), and nemolizumab 30 mg Q4W (7.9%).

For IGA 0/1, dupilumab 300 mg QW achieved the greatest response rate (26.8%), followed closely by dupilumab 300 mg Q2W (26.3%), lebrikizumab 250 mg Q2W (18.7%), tralokinumab 300 mg Q2W (12.7%), and nemolizumab 30 mg Q4W (11.4%).

For PP-NRS4, dupilumab 300 mg QW demonstrated the highest estimated response rate (39.1%), followed by Dupilumab 300 mg Q2W (31.1%) and nemolizumab 30 mg Q4W (23.9%). Lebrikizumab 250 mg Q2W (19.2%) and tralokinumab 300 mg Q2W (11.3%) had the lowest response rate.

These descriptive estimates should not be interpreted as evidence of equivalence or statistically credible differences between active treatments. Detailed data are provided in Supplementary Table 1.

Safety Outcomes

Within the inherent limitations of cross study comparisons of infrequently occurring adverse events, the overall incidence of adverse events was comparable between biologic therapies and placebo, with most events being mild to moderate in severity (Table 3). Serious adverse events were uncommon and treatment discontinuations due to safety concerns occurred infrequently across all treatment groups. Conjunctivitis was reported more often with dupilumab and tralokinumab than with placebo, whereas herpes infections remained rare. No biologic demonstrated a consistent increase in serious infections, and deaths were either absent or uncommon across the trials. Overall, all evaluated biologic therapies exhibited acceptable and predictable safety profiles, with no unexpected safety signals identified.

DISCUSSION

This Bayesian network meta-analysis compared the efficacy of approved biologic therapies administered with background topical therapy for moderate-to-severe AD using multiple clinically relevant Week 16 outcomes. Dupilumab, tralokinumab, lebrikizumab, and nemolizumab were selected because they represent the only biologic agents approved in the United States, United Kingdom, Europe, and Japan for moderate-to-severe AD in combination with TCS. Dupilumab, tralokinumab, and lebrikizumab are approved both as monotherapy and in combination with TCS, whereas nemolizumab was not evaluated as monotherapy in pivotal trials and is therefore approved

only for use with background TCS. Across all skin clearance and itch reduction endpoints (EASI 75, EASI 90, IGA 0/1, and PP NRS4) evaluated at Week 16, dupilumab consistently demonstrated the highest numerical efficacy estimates, with QW and the approved Q2W dosing regimens ranking first in Bayesian estimates, SUCRA rankings, and observed response rates. Dupilumab 300 mg Q2W produced the greatest probability of achieving EASI 75, whereas the 300 mg QW regimen ranked highest for EASI 90, IGA 0/1, and PP NRS4 improvement. These findings indicate that both evaluated dupilumab dosing schedules provide robust clinical benefit, with only minor numerical differences between them.

Lebrikizumab consistently ranked second (after the two dupilumab regimens) across objective skin clearance outcomes and demonstrated efficacy intermediate between dupilumab and tralokinumab. Although indirect comparisons did not identify statistically significant differences between active biologics, ranking analyses consistently favored lebrikizumab over tralokinumab and nemolizumab for EASI and IGA responses. These results suggest that selective IL 13 inhibition, particularly higher affinity IL 13 inhibition with lebrikizumab, provides substantial improvement in skin inflammation, consistent with mechanistic expectations, although its estimated efficacy remained lower than that of dupilumab, which provides dual IL 4/IL 13 blockade [12, 17, 22-24].

Among the four approved biologics included in this study, nemolizumab ranked lowest for skin clearance outcomes (EASI 75, EASI 90, and IGA), yet ranked second (after dupilumab) for itch improvement. This pattern is biologically plausible given that nemolizumab targets IL 31 receptor α, a pathway directly involved in pruritus rather than generalized skin inflammation. Despite more modest effects on objective skin clearance, nemolizumab may offer particular value in appropriately selected patients with severe pruritus who have a suboptimal efficacy or safety response to dupilumab, given the prominent and burdensome role of itch in AD [25-31].

Tralokinumab consistently ranked below dupilumab and lebrikizumab across efficacy outcomes. Nevertheless, it demonstrated clinically meaningful improvements over placebo with an acceptable safety profile, supporting its role as an effective treatment option for moderate-to-severe AD.

Our findings align with previous pairwise meta-analyses and indirect treatment comparisons reporting superior efficacy of dupilumab among currently approved biologic monotherapies for

moderate-to-severe AD [30-34]. Unlike earlier analyses, the present study focused exclusively on approved biologic therapies administered with background topical therapy and evaluated at a common 16-Week endpoint. This approach reduced clinical heterogeneity arising from differences in treatment conditions and assessment timing, thereby improving comparability across interventions. The comparatively stronger antipruritic efficacy observed with nemolizumab is consistent with mechanistic and clinical evidence demonstrating the central role of IL 31 signaling in itch transmission [35, 36]. Previous phase 3 trials have shown rapid itch improvement with nemolizumab, even when EASI responses are less pronounced than those observed with dupilumab [27-29]. Similarly, our observation that lebrikizumab performs between dupilumab and tralokinumab is supported by clinical evidence suggesting that higher-affinity selective IL 13 inhibition results in greater clinical responses than IL 13 blockade with tralokinumab alone [37].

These findings have several important clinical implications. Dupilumab may be considered the preferred biologic option for most AD patients, including those with high lesion burden, high pruritus burden, or both, because it consistently produced the highest numerical estimates and rankings across evaluated outcomes when administered with background topical therapy and as monotherapy [32, 38]. Both evaluated dosing regimens demonstrated comparable performance, suggesting that the standard every two week maintenance regimen may provide efficacy similar to weekly dosing over the 16 week assessment period. Lebrikizumab represents an intermediate option, offering strong efficacy for objective disease control while maintaining a favorable safety profile. Tralokinumab remains an effective alternative, particularly in patients unsuitable for other biologic therapies. Lebrikizumab may be particularly suitable for patients with high lesion burden who experience suboptimal efficacy or tolerability with dupilumab. For patients in whom itch is the predominant symptom, nemolizumab may represent an attractive therapeutic option because it ranked higher than lebrikizumab and tralokinumab for PP NRS4 response [39-41]. Given that itch is a major determinant of impaired sleep, quality of life, and psychological burden in AD, therapies targeting IL 31 may provide clinically meaningful benefit even when improvements in skin clearance are comparatively modest [42].

Across the evaluated biologics, safety outcomes in combination-therapy trials were broadly consistent with their established safety profiles. Overall adverse-event frequencies were generally comparable between biologic and placebo groups, with most events being mild or moderate in

severity. Serious adverse events and treatment discontinuations were uncommon. Consistent with previous studies of biologics targeting the IL-4/IL-13 pathway, ocular adverse events particularly conjunctivitis were reported more frequently with dupilumab, tralokinumab, and lebrikizumab than with placebo; however, these events were generally mild or moderate, manageable, and rarely resulted in treatment discontinuation. Herpes viral infections were infrequent, although a numerical increase was observed with lebrikizumab in the ADhere trial [43]. No consistent safety signal for serious infections or mortality was identified across the evaluated biologics. Collectively, these findings support the generally predictable and acceptable short-term safety profiles of these agents, although longer-term surveillance remains important. Interpretation of safety outcomes, particularly infrequently occurring AEs, should consider the inherent limitations of cross trial safety reporting, including variation in definitions, ascertainment, and reporting thresholds.

Real world experience varies substantially across biologics, reflecting differences in time on the market. Dupilumab, approved in 2017 and supported by nearly a decade of post marketing data, remains the most extensively characterized agent, with long term safety evidence across diverse populations and multiple atopic comorbidities. Tralokinumab, with over four years of market availability, has accumulated a moderate evidence base that aligns with its clinical trial performance. In contrast, lebrikizumab and nemolizumab, approved in 2024, have more limited real world exposure, and their safety datasets remain comparatively smaller. Thus, while clinical trial safety profiles for lebrikizumab and nemolizumab are reassuring, continued surveillance and longer term data will be essential to fully define their risk–benefit profiles.

Importantly, shorter time since approval does not necessarily imply lower clinical adoption or commercial performance. Newer agents may achieve rapid uptake depending on therapeutic positioning, unmet need, payer dynamics, formulary access, and perceived advantages in efficacy or tolerability. As real world use expands, these factors will shape the evolving safety and effectiveness profiles of lebrikizumab and nemolizumab, complementing the controlled evidence generated in pivotal trials.

Although the FDA has not issued formal guidance defining the development pathway for systemic dermatologic therapies, there remains a longstanding regulatory expectation that pharmaceutical

sponsors will submit NDAs or BLAs supported by substantial evidence of effectiveness derived from two or more adequate and well controlled trials, usually replicate in design. For biologics and JAK inhibitors in AD, the FDA has consistently required two monotherapy trials comparing the investigational agent with placebo, along with an additional study evaluating the agent in combination with background TCS. Although this three trial structure is not codified in formal guidance, it remains a consistent and deeply embedded FDA review practice. Updated FDA guidance acknowledges that a single pivotal trial may be sufficient when accompanied by confirmatory evidence from other sources, including related controlled trials, data supporting a related indication, evidence from drugs within the same pharmacologic class, mechanistic or biological support, and early phase clinical data. However, in practice, the evidentiary conditions required to waive the traditional replicate trial expectation are exceedingly difficult to satisfy, and the FDA has continued to apply the conventional multi trial standard in drug development [44, 45]. A landmark 2026 analysis by Hediger et al. in JAMA Health Forum reported that despite policy pressure and regulatory reforms intended to accelerate patient access to new therapeutics, the median interval from initiation of clinical development to reimbursement has shown minimal variation since 2014 [46].

The continued insistence on two monotherapy trials plus a TCS background study is increasingly problematic, particularly for agents within the same pharmacologic class. Moderate to severe AD combined with strict study enrolment criteria require large, multinational trials to enroll adequate numbers of eligible participants. Given the limited global patient pool and substantial competition among ongoing AD studies, mandating replicate trials increases development costs, prolongs time to market, introduces operational challenges, and raises concerns regarding clinical equipoise. Moreover, well designed monotherapy trials of biologics and systemic JAK inhibitors consistently yield efficacy results directionally similar to those observed in combination with TCS studies. Trials incorporating background TCS also demonstrate markedly higher placebo responses compared with monotherapy designs, adding unnecessary complexity and burden to clinical development programs and further constraining the ability of sponsors to complete adequately powered studies in a timely way [47].

This study has several strengths. First, only phase 3 randomized controlled trials evaluating approved biologic therapies administered with background topical treatment were included,

minimizing heterogeneity from early phase investigations, experimental agents, and monotherapy only designs. Second, all efficacy endpoints were harmonized at a common Week 16 assessment, reducing variability introduced by differing follow up durations across trials. Third, the Bayesian analytic framework enabled simultaneous estimation of direct and indirect treatment effects, treatment rankings, and absolute response probabilities while appropriately incorporating uncertainty through posterior distributions. Fourth, multiple clinically meaningful outcomes, including EASI 75, EASI 90, IGA 0/1, and PP NRS4, were examined, providing a comprehensive evaluation of therapeutic performance. Finally, the inclusion of trials conducted across numerous global regions enhances the external validity of the findings, supporting applicability across diverse patient populations and clinical settings. Together, these methodological features strengthen both the internal rigor and generalizability of this network meta-analysis.

Several limitations should be acknowledged. First, the treatment network relied predominantly on placebo controlled trials, increasing dependence on indirect evidence. With any indirect comparison, the possibility remains that unmeasured or unreported factors influencing treatment response could contribute residual bias, even after accounting for observed baseline differences. Second, the analysis was based on published aggregate level data rather than individual patient data, which can introduce forms of bias more difficult to control compared with analyses using patient level datasets. Third, despite broadly comparable trial populations, differences in participant demographics, geographic and environmental exposures, baseline disease severity, prior treatment exposure, rescue medication use, and other unmeasured biologic or immunologic factors likely contributed residual confounding and may have introduced clinical heterogeneity, posing challenges for fully satisfying the transitivity assumption.

Fourth, pharmacologic evaluations conducted alongside background topical therapy, particularly TCS, introduce additional heterogeneity due to variation in formulation, potency, application frequency, treated body surface area, anatomical sites, and concomitant use of calcineurin inhibitors. These factors contribute to substantially elevated placebo response in AD trials. Prior modeling work has shown that allowing concomitant TCS can markedly amplify placebo performance, with studies permitting background therapy demonstrating approximately a 1.8 fold increase in EASI 75 placebo rates compared with trials that prohibit topical agents [47]. This enhanced placebo activity complicates interpretation of treatment effects and remains an important

source of variability across studies [48]. Fifth, because efficacy assessments were limited to the 16 week induction period, these findings cannot be extrapolated to long term maintenance therapy or relapse prevention. Most biologics demonstrate continued improvement well beyond the initial treatment window, often through 52 weeks or longer; therefore, the present analysis cannot fully characterize sustained response, deepening of clinical benefit, complete skin clearance, relapse dynamics, or long term safety, key considerations in a chronic, relapsing disease. Moreover, once placebo groups are discontinued and participants are re randomized or transitioned to active therapy, the network loses its shared comparator, restricting the validity of indirect comparisons during extended follow up. This structure implicitly assumes that all biologics, including those with distinct mechanisms of action, follow comparable long term trajectories, an assumption that may not hold and further limits interpretation of maintenance phase differences.

Sixth, safety outcomes were summarized descriptively rather than quantitatively because adverse event definitions and reporting methods differed substantially across trials. Cross trial variation in AE definitions, ascertainment, and reporting practices further limits the comparability of safety outcomes. Seventh, although Bayesian ranking provides useful comparative information, SUCRA values should not be interpreted as definitive measures of clinical superiority, particularly when CrIs overlap and indirect comparisons fail to demonstrate statistically credible differences. Finally, patient reported outcomes beyond itch, including quality of life, sleep disturbance, and work productivity, were not consistently reported across studies and therefore could not be included in the quantitative analyses.

CONCLUSION

Among currently approved biologic therapies administered with background topical therapy for moderate-to-severe AD, dupilumab demonstrated the highest numerical efficacy estimates across objective skin-clearance and patient-reported itch outcomes at Week 16, consistent with a recent Bayesian network analysis of targeted, systemic biologics given as monotherapy for moderate to severe AD. Lebrikizumab and tralokinumab ranked second and third, respectively, for skin-clearance outcomes, whereas nemolizumab ranked second for itch but last for lesion reduction, reflecting its distinct mechanism of IL-31 receptor inhibition. Although indirect comparisons did not demonstrate statistically credible differences between active treatments, Bayesian ranking

consistently favored dupilumab across efficacy endpoints. These findings provide comparative evidence to support individualized biologic selection based on therapeutic priorities, particularly the balance between skin clearance and itch relief. Future head-to-head randomized trials and long-term comparative effectiveness studies are needed to confirm these findings and better inform treatment sequencing in clinical practice.

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TABLES

Table 1. Characteristics of Included Randomized Controlled Trials

Author	Trial Name	Phase	Registration	Country/Region	Study Design	Intervention	Comparator	Sample Size
Blauvelt et al. 2017	LIBERTY AD CHRONOS	Phase III	NCT02260986	Multinational (Australia, Canada, Czech Republic, Hungary, Italy, Japan, Netherlands, New Zealand, Poland, Romania, South Korea, Spain, UK, USA)	Multicenter, randomized, double-blind, placebo-controlled, parallel-group trial	Dupilumab 300 mg QW + TCS; Dupilumab 300 mg Q2W + TCS	Placebo + TCS	740
Silverberg et al. 2022	ECZTRA 3	Phase III	NCT03363854	Europe and North America (68 sites)	Randomized, double-blind, placebo-controlled, multicenter trial (2:1 randomization)	Tralokinumab 300 mg Q2W+ TCS	Placebo + TCS	380
Silverberg et al. 2024	ARCADIA 1	Phase III	NCT03985943	Multinational (14 countries; 161 centers)	Randomized, double-blind, placebo-controlled, parallel-group trial	Nemolizumab 30 mg SC every 4 weeks (60 mg loading dose) + TCS ± TCI	Placebo + TCS ± TCI	941

Silverberg et al. 2024	ARCADIA 2	Phase III	NCT03989349	Multinational (11 countries; 120 centers)	Randomized, double-blind, placebo-controlled, parallel-group trial	Nemolizumab 30 mg SC every 4 weeks (60 mg loading dose) + TCS ± TCI	Placebo + TCS ± TCI	787
Simpson et al. 2023	ADhere	Phase III	NCT04250337	Germany, Poland, Canada, USA	Multicenter, randomized, double-blind, placebo-controlled, parallel-group trial (2:1 randomization)	Lebrikizumab 500 mg SC at baseline and Week 2 (loading doses), followed by 250 mg SC every 2 weeks (Q2W) plus low-/mid-potency TCS	Placebo Q2W plus low-/mid-potency TCS	211

Abbreviations: TCS, topical corticosteroids; TCI, topical calcineurin inhibitors; SC, subcutaneous; QW, once weekly; Q2W, every 2 weeks; RCT, randomized controlled trial; NR, not reported.

Table 2. Baseline Characteristics of Included Patients

Study	Treatment	Sample Size	Mean Age (years)	Female (%)	Disease Duration (years)	Baseline EASI score	Baseline IGA 3 (%) / IGA 4 (%)	Baseline BSA (%)	Baseline PP-NRS
Blauvelt et al.2017	Dupilumab 300 mg QW	106	40.5	42	28	30.9	50 / 50	58.8	7.7
	Dupilumab 300 mg Q2W	319	34	40	26	29	46 / 54	52	7.4
	Placebo	315	34	39	26	29.6	47 / 53	55	7.6
Silverberg et al. 2022	Tralokinumab 300	253	39.8	50.6	28	28.8	53.8 / 45.8	47.6	7.7
	Placebo	127	37.7	33.9	28.7	30.4	52 / 47.2	49	7.9
Silverberg et al. 2024	Nemolizumab 30 mg (ARCADIA 1)	620	33.5 ± 15.9	48	NR	27.8 ± 10.6	71 / 29	44.9 ± 19.9	7.2 ± 1.4
	Placebo	321	33.3 ± 15.6	45	NR	27.1 ± 9.4	74 / 26	43.8 ± 18.7	7.2 ± 1.4
Silverberg et al. 2024	Nemolizumab 30 mg (ARCADIA 2)	522	34.9 ± 17.7	52	NR	27.4 ± 10.8	67 / 33	44.6 ± 19.4	7.0 ± 1.5
	Placebo	265	35.2 ± 17.0	51	NR	27.6 ± 10.9	70 / 30	45.0 ± 19.3	7.2 ± 1.5
Simpson et al. 2023	Lebrikizumab 250 mg	145	37.5	48.3	21	27.7	67.6 / 32.4	40.4	7.3
	Placebo	66	36.7	50	21.2	26.4	72.7 / 27.3	38.2	6.8

Footnotes:

Data are presented as mean ± standard deviation (SD), median (interquartile range), or number (%) as reported in the original studies.

Abbreviations: EASI, Eczema Area and Severity Index; IGA, Investigator's Global Assessment; BSA, body surface area; PP-NRS, Peak Pruritus Numeric Rating Scale; NR, not reported.

Table 3. Safety Outcomes

Study	Treatment	Any AE n (%)	Serious AE n (%)	Serious Infection n (%)	Discontinuation due to AE n (%)	Conjunctivitis n (%)	Herpes Infection* n (%)	Death
Blauvelt et al.2017	Dupilumab 300 mg Q2W	97 (88)	4 (4)	NR	0 (0)	31 (28)	8 (7)	0
	Dupilumab 300 mg QW	261 (83)	9 (3)	NR	11 (3)	54 (17)	22 (7)	0
	Placebo	266 (84)	16 (5)	NR	24 (8)	26 (8)	25 (8)	0
Silverberg et al. 2022	Tralokinumab 300 mg Q2W	180 (71.4)	2 (0.8)	4 (1.6)	6 (2.4)	33 (13.1)	1 (0.4)	0
	Placebo	84 (66.7)	4 (3.2)	7 (5.6)	1 (0.8)	7 (5.6)	1 (0.8)	0
Silverberg et al. 2024 (ARCADIA 1)	Nemolizumab 30 mg (ARCADIA 1)	306 (50)	6 (1)	NR	11 (1.8)	NR	NR	0
	Placebo	146 (45)	4 (1)	NR	13 (4.0)	NR	NR	0
Silverberg et al. 2024 (ARCADIA 2)	Nemolizumab 30 mg (ARCADIA 2)	215 (41)	13 (3)	3 (0.6)	18 (3.5)	NR	NR	0
	Placebo	117 (44)	3 (1)	1 (0.4)	3 (1.1)	NR	NR	0
Simpson et al. 2023	Lebrikizumab 250 mg	63 (43.4)	2 (1.4)	0 (0.0)	3 (2.1)	7 (4.8)	5 (3.4)	0
	Placebo	23 (34.8)	1 (1.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.5)	0

Footnotes:
Data are presented as number of patients with events (%).
*Herpes infection includes herpes simplex, eczema herpeticum, herpes zoster, and other herpes virus infections, as defined by the individual trials.
Abbreviations: AE, adverse event; NR, not reported.

TITLES OF FIGURES

Figure 1. PRISMA 2020 flow diagram illustrating the study selection process for the Bayesian network meta-analysis.

Figure 2. Network plot of treatment comparisons included in the Bayesian network meta-analysis. It shows the evidence structure for placebo-controlled comparisons of dupilumab 300 mg QW, dupilumab 300 mg Q2W, lebrikizumab 250 mg Q2W, tralokinumab 300 mg Q2W, and nemolizumab 30 mg Q4W with background topical therapy in patients with moderate to severe atopic dermatitis. Node size is proportional to the number of participants receiving each intervention, and line thickness reflects the number of direct comparisons available between treatments. Placebo with background topical therapy served as the common comparator connecting all treatment nodes.

Figure 3. Bayesian Network Meta-analysis of EASI-75 Response. Dupilumab 300 mg Q2W demonstrated the greatest efficacy, followed by dupilumab 300 mg QW, lebrikizumab 250 mg Q2W, tralokinumab 300 mg Q2W, and nemolizumab 30 mg Q4W. Only dupilumab Q2W demonstrated a credible benefit over placebo. Treatment effects are reported as ORs with 95% CrIs. OR >1 favors treatment. The dashed vertical line at OR = 1 indicates no difference.

Figure 4. Bayesian Network Meta-analysis of EASI-90 Response. Dupilumab 300 mg QW demonstrated the greatest efficacy, followed by dupilumab 300 mg Q2W, lebrikizumab 250 mg Q2W, tralokinumab 300 mg Q2W, and nemolizumab 30 mg Q4W. Only dupilumab QW demonstrated a credible benefit over placebo. Treatment effects are reported as ORs with 95% CrIs. OR >1 favors treatment. The dashed vertical line at OR = 1 indicates no difference.

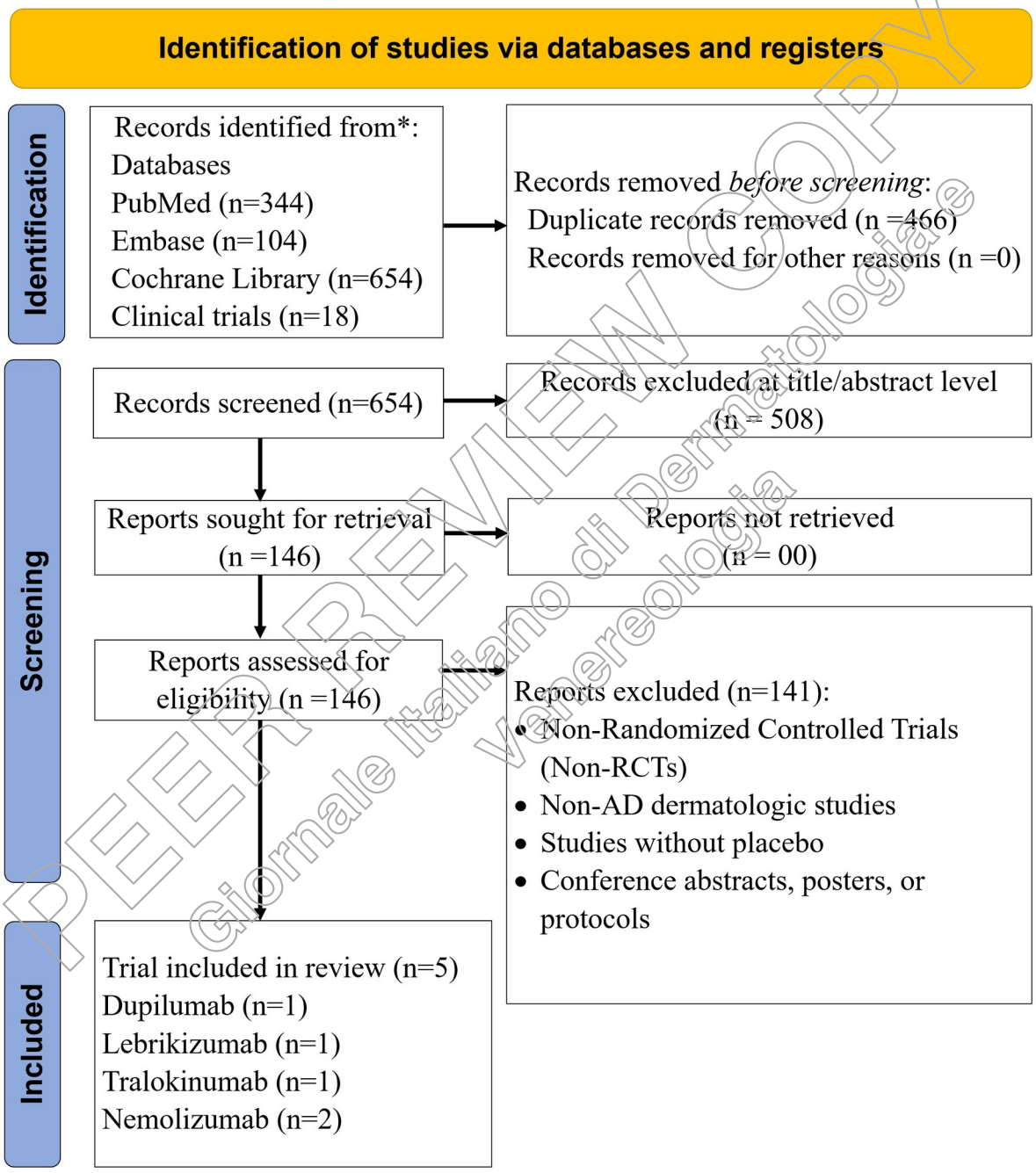
Figure 5. Bayesian Network Meta-analysis of IGA 0/1 Response. Dupilumab 300 mg QW demonstrated the greatest efficacy, closely followed by dupilumab 300 mg Q2W, lebrikizumab 250 mg Q2W, tralokinumab 300 mg Q2W, and nemolizumab 30 mg Q4W. Both dupilumab regimens demonstrated credible benefits over placebo. Treatment effects are reported as ORs with 95% CrIs. OR >1 favors treatment. The dashed vertical line at OR = 1 indicates no difference.

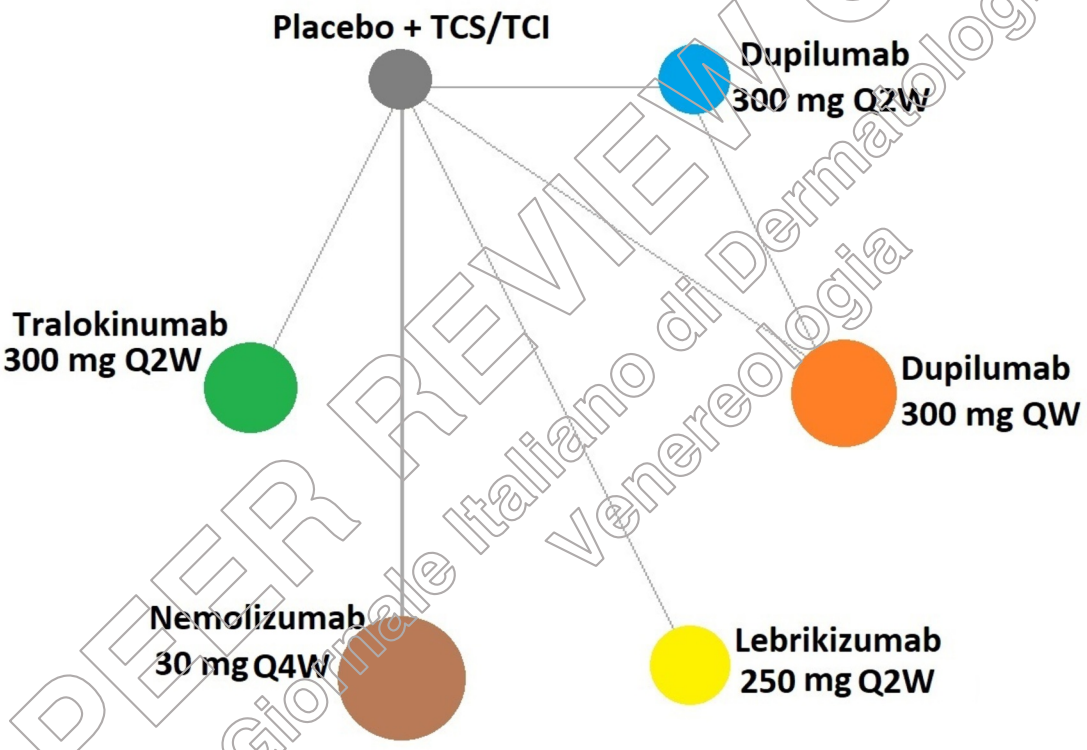
Figure 6. Bayesian Network Meta-analysis of PP-NRS ≥4-Point Improvement. Dupilumab 300 mg QW demonstrated the greatest improvement, followed by dupilumab 300 mg Q2W, nemolizumab 30 mg Q4W, lebrikizumab 250 mg Q2W, and tralokinumab 300 mg Q2W. Credible benefits over placebo were observed for dupilumab QW and nemolizumab Q4W. Treatment effects are reported as ORs with 95% CrIs. OR >1 favors treatment. The dashed vertical line at OR = 1 indicates no difference.

Figure 7. League table of pairwise comparisons. Dupilumab 300 mg Q2W demonstrated a credible benefit over placebo. Although the effect estimates numerically favored dupilumab over the other active treatments, no credible differences were observed between active treatments, as all corresponding 95% CrIs crossed the null value (OR = 1). Values are posterior median ORs with 95% CrIs. Each cell compares the row treatment with the column treatment; OR >1 favors the row treatment, whereas OR <1 favors the column treatment.

Figure 8. Surface under the cumulative ranking curve (SUCRA) rankings for efficacy outcomes. Bar charts displaying SUCRA values ranking each treatment's relative efficacy across key clinical endpoints. Higher SUCRA scores indicate a greater probability of being among the most effective therapies. EASI-75, Eczema Area and Severity Index 75% improvement; EASI-90, Eczema Area and Severity Index 90% improvement, IGA-AD, Investigator's Global Assessment for Atopic Dermatitis, PP-NRS, Peak Pruritus Numerical Rating Scale; QW, every week, Q2W, every two weeks; Q4W, every four weeks

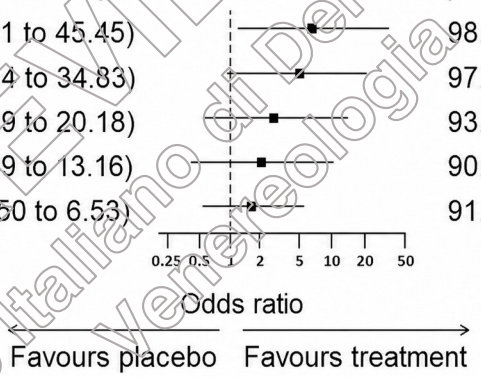
Figure 9. Observed response rates for biologic therapies in combination with topical therapy across efficacy outcomes. Bar charts of observed values across key clinical endpoints. EASI-75, Eczema Area and Severity Index 75% improvement; EASI-90, Eczema Area and Severity Index 90% improvement; IGA-AD, Investigator's Global Assessment for Atopic Dermatitis, PP-NRS, Peak Pruritus Numerical Rating Scale; QW, every week, Q2W, every two weeks; Q4W, every four weeks.

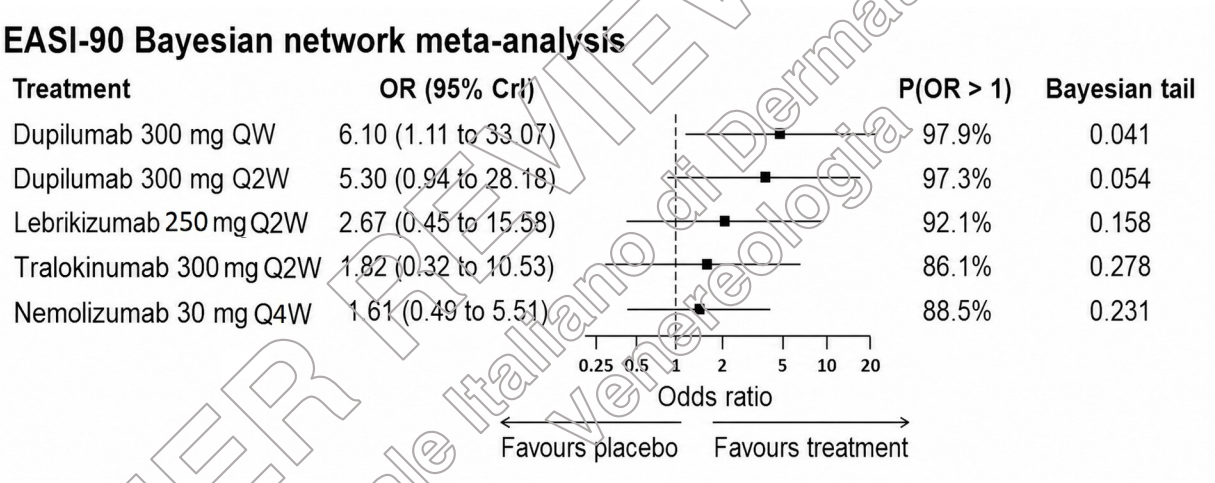




EASI-75 Bayesian network meta-analysis

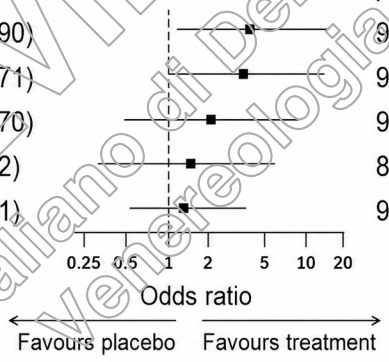
Treatment	OR (95% CrI)	P(OR > 1)	Bayesian tail
Dupilumab 300 mg Q2W	7.46 (1.21 to 45.45)	98.1%	0.038
Dupilumab 300 mg QW	5.90 (0.94 to 34.83)	97.3%	0.054
Lebrikizumab 250 mg Q2W	3.20 (0.49 to 20.18)	93.5%	0.129
Tralokinumab 300 mg Q2W	2.29 (0.39 to 13.16)	90.3%	0.193
Nemolizumab 30 mg Q4W	1.79 (0.50 to 6.53)	91.0%	0.179





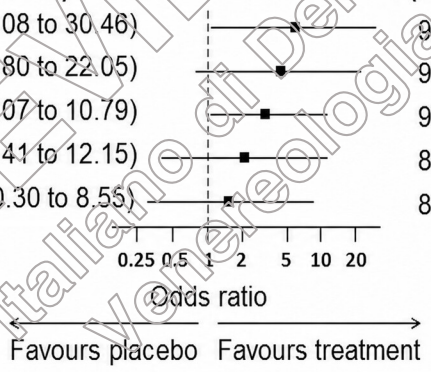
IGA response: Bayesian network meta-analysis

Treatment	OR (95% CrI)	P(OR > 1)	Bayesian tail
Dupilumab 300 mg QW	4.56 (1.13 to 18.90)	97.9%	0.043
Dupilumab 300 mg Q2W	4.46 (1.05 to 18.71)	97.7%	0.046
Lebrikizumab 250 mg Q2W	2.45 (0.57 to 10.70)	92.8%	0.143
Tralokinumab 300 mg Q2W	1.81 (0.41 to 7.52)	88.2%	0.236
Nemolizumab 30 mg Q4W	1.71 (0.63 to 4.51)	92.0%	0.160



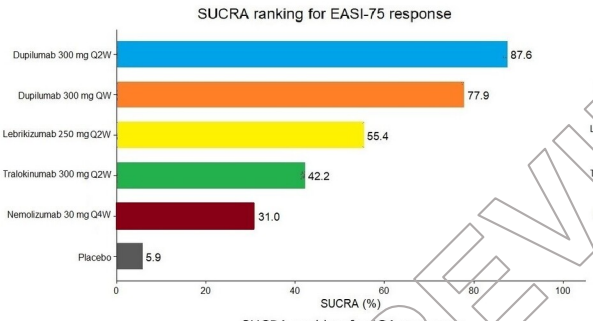
PP-NRS response: Bayesian network meta-analysis

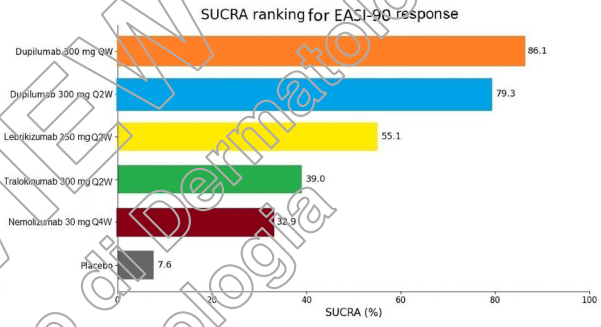
Treatment	OR (95% CrI)	P(OR > 1)	Bayesian tail
Dupilumab 300 mg QW	5.87 (1.08 to 30.46)	97.8%	0.044
Dupilumab 300 mg Q2W	4.26 (0.80 to 22.05)	96.5%	0.071
Nemolizumab 30 mg Q4W	3.32 (1.07 to 10.79)	97.9%	0.042
Lebrikizumab 250 mg Q2W	2.26 (0.41 to 12.15)	89.9%	0.202
Tralokinumab 300 mg Q2W	1.62 (0.30 to 8.55)	83.3%	0.333

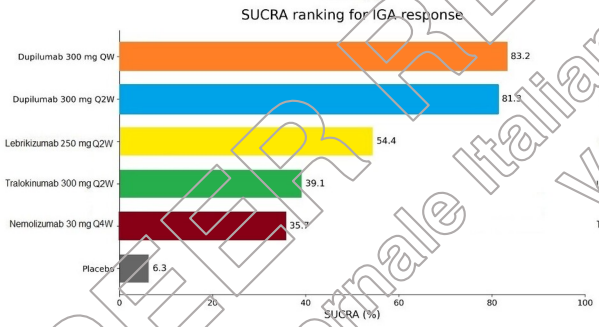


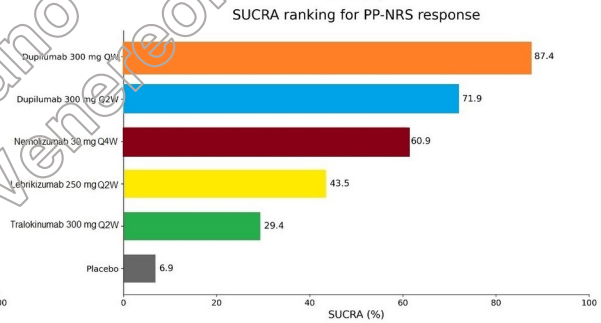
Treatment	Dupilumab 300 mg QW	Dupilumab 300 mg Q2W	Placebo	Tralokinumab 300 mg Q2W	Nemolizumab 30 mg Q4W	Lebrikizumab 250 mg Q2W
Dupilumab 300 mg QW	—					
Dupilumab 300 mg Q2W	1.26 (0.21 to 7.83)	—				
Placebo	0.17 (0.03 to 1.06)	0.13 (0.02 to 0.82)	—			
Tralokinumab 300 mg Q2W	0.39 (0.03 to 4.75)	0.31 (0.02 to 3.42)	2.29 (0.39 to 13.16)	—		
Nemolizumab 30 mg Q4W	0.30 (0.04 to 2.82)	0.24 (0.03 to 2.07)	1.79 (0.50 to 6.53)	0.78 (0.09 to 7.20)	—	
Lebrikizumab 250 mg Q2W	0.54 (0.04 to 7.45)	0.43 (0.03 to 5.78)	3.20 (0.49 to 20.18)	1.39 (0.11 to 19.18)	1.78 (0.19 to 16.61)	—

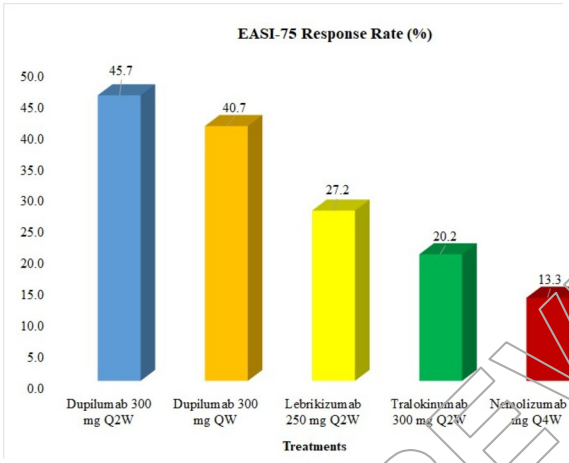
Values are posterior median odds ratios with 95% credible intervals. Each cell compares the row treatment with the column treatment. OR > 1 favours the row treatment.

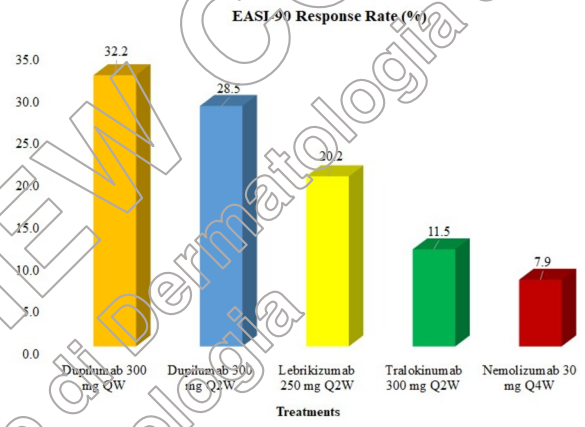


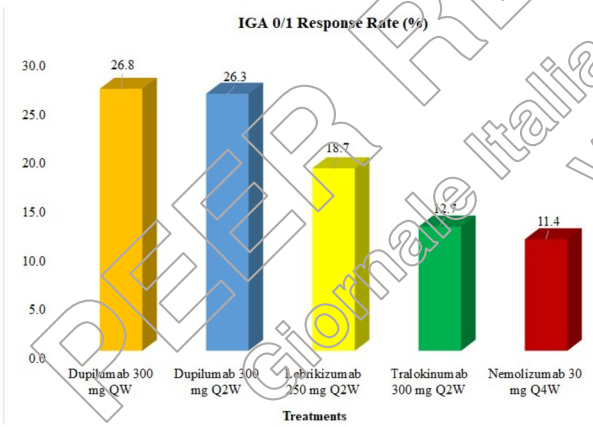


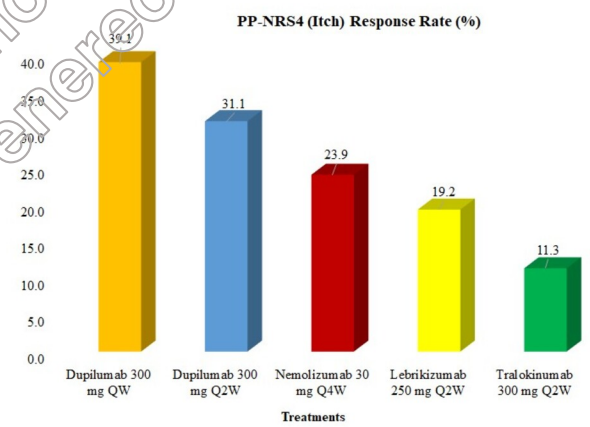












Supplementary Digital Material

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