Review Article

Efficacy and Safety of Lebrikizumab in Atopic Dermatitis: A Systematic Review and Meta-Analysis

Abstract

Background: Atopic Dermatitis (AD) is a long-lasting dermatological condition that leads to skin irritation and inflammation. In cases of severe cases of AD biological therapy may be warranted. In this systematic review and meta-analysis, we aim to assess the efficacy and safety of Lebrikizumab, an IL-13 immunomodulator.

Methodology: A systematic search was used in the following databases Medline, Scopus, Clinical Trials.gov registry (CT.gov), EBSCO, Science Direct, Cochrane Central Register of Controlled Trials (CENTRAL), and Google Scholar. The efficacy of Lebrikizumab was evaluated by using some measures such as Investigator's Global Assessment (IGA), Body Surface Area (BSA), and Eczema Area and Severity Index (EASI). The measures namely serious adverse events (SAEs), and non-serious adverse events (NSAEs) were used to assess the safety. The risk of bias was determined by the Revised Cochrane risk of bias tool.

Results: Four randomized controlled trials (RCTs) were included in our meta-analysis with a total of 1,686 patients who had taken lebrikizumab (n =1,168) compared with placebo (n= 518). The total analysis demonstrated a decrease in the area and severity of eczema as measured by EASI when using lebrikizumab, this decrease was statistically significant compared to placebo (mean difference (MD): -25.60, 95% CI [-38.01, -13.18], $P < 0.0001$), statistically significant enhancement in the Change of BSA with lebrikizumab compared to placebo (MD: -9.81, 95% CI [-15.39, -4.23], $P < 0.0006$), and significant enhancement in the EASI 75 score with lebrikizumab compared to placebo (Risk Ratio (RR):2.60, 95% CI [2.17, 3.13], $P < 0.00001$). Lebrikizumab did not correlate significantly with the incidence of NSAEs and SAEs as concluded by the pooled analysis of safety.

Conclusion: Lebrikizumab has demonstrated promise as a treatment option for AD. It has shown significant effectiveness across various measures and has exhibited a favourable safety profile. Future research is required to evaluate long-term safety and efficacy.

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Systematic review registration: CRD42024456389.

Keywords: Atopic dermatitis, Eczema, Lebrikizumab, anti-IL-13

Introduction

Atopic Dermatitis (AD) is a long-lasting dermatological condition that leads to skin irritation and inflammation (1,2). AD affects both children and adults but is more common in children usually occurring between the ages of 3 to 6 months (1). The incidence of AD has increased through the years, affecting 15-20 % of the pediatric population and 1-3 % of adults (1,3). AD is a complex disease with various factors contributing to its pathophysiology. The exact cause of AD is not fully understood but a combination of genetic, immunological, microbial, and environmental factors is associated with AD development. The inside-out hypothesis suggests that cutaneous inflammation occurs before barrier impairment in AD. Inflammatory conditions weaken the skin's barrier by reducing the production of a protein called filaggrin, which is crucial for maintaining skin integrity. This disruption of the barrier can enable allergens and bacteria to penetrate the skin, leading to the development of AD. On the other hand, the outside-in hypothesis proposes that the impaired skin barrier precedes AD and is necessary for immune dysregulation to occur. When the skin barrier is disrupted, it can result in heightened immune responses, specifically Th2 responses, which contribute to inflammation in AD. Other factors, including genetic variations and environmental influences, may contribute to the development of AD in individuals without filaggrin mutations (1,4).

AD may result from the downregulation or mutation of the filaggrin (FLG) gene, which is necessary for healthy skin barrier function as it encodes the protein filaggrin, which is responsible for making a strong barrier matrix and may increase the skin's susceptibility to immunological dysregulation (1,5). Genetic factors and family history of atopic diseases such as asthma and allergic rhinitis, are important risk factors for developing atopic dermatitis (1). Immune dysfunction in AD is biphasic. In the acute phase, TH2 immune response is dominant while TH1 is dominant in the chronic phase (2,3). Moreover, environmental factors like allergens, pollutants, and irritants may also trigger atopic dermatitis symptoms (3). Current management of AD consists of avoidance of triggers, emollients, topical corticosteroids,

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topical calcineurin inhibitors, and phosphodiesterase-4 inhibitors. In severe cases, oral corticosteroids, immunosuppressants, and biological agents may be used(6–8).

Lebrikizumab is an IgG4 monoclonal antibody targeting IL-13 and inhibiting the formation of IL-13Ra1 (IL-13 receptor alpha 1)/IL-4Ra (IL-4 receptor alpha) receptor complex. IL-13 plays a vital role in provoking inflammation and causing dysfunction of the skin barrier in atopic dermatitis(9–11). This induces the symptoms of AD to appear such as redness, itching, and skin thickening. IL-13 is produced by many different cells such as TH2 cells, eosinophils, and mast cells in response to triggers. Therefore, lebrikizumab downregulates the signalling pathway and the effects of IL-13 which are an important contributor to the disease pathogenesis. It can be used for treating adults and patients older than 12 with moderate to severe atopic dermatitis(11). It's used in individuals who are candidates for systemic therapy due to the non-effectiveness of the topical treatments. The most common side effects include conjunctivitis and injection site reaction (9,10).

Materials and methods:

Our study was registered before a preliminary search in alignment with PROSPERO. It utilized the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) checklist.

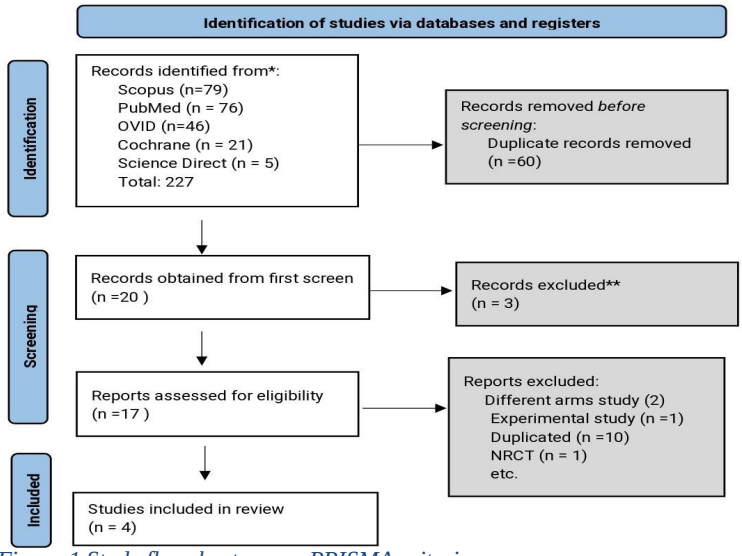

Figure 1 Study flowchart as per PRISMA criteria

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Eligibility criteria

Our study included all patients who were treated with lebrikizumab for atopic dermatitis as monotherapy or in combination with other treatment modalities. We excluded all studies discussing treatments of atopic dermatitis other than lebrikizumab, Alternative uses of lebrikizumab other than atopic dermatitis treatment, irrelevant articles, and non-English articles.

Search strategy

We systematically searched Medline, Scopus, Clinical Trials.gov registry (CT.gov), EBSCO, Science Direct, Cochrane Central Register of Controlled Trials (CENTRAL), and Google Scholar databases without any restriction on date or language. References of the included RCTs were inspected for relevant RCTs that were missed during the systematic search process. The search was conducted by using the keywords “Atopic dermatitis”, “Eczema”, “Lebrikizumab”, “Efficacy”, and “safety”.

Study selection and data extraction

Two reviewers independently performed title and abstract screening by using Rayyan, full-text screening, and data extraction of RCTs that matched the eligibility criteria. Any conflict was resolved third author’s opinion. Cochrane Risk of Bias Tool 1 was used to assess the included studies.

Results:

Literature Search Results

A total of 227 articles had been selected for title and abstract screening. Following this initial screening process, only five articles were found to meet the specific criteria set for our study. These five articles were then subjected to a full screening process. To visualize the flow of the study selection process PRISMA flowchart (Figure 1).

Characteristics of the Included Studies

Four studies were included in our meta-analysis NCT04250337, NCTO4146363, NCTO4178967, and NCTO3443024, with a total of 1,686 patients who had taken lebrikizumab for atopic dermatitis compared with placebo (lebrikizumab group n =1,168 and placebo group n=

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518)(9,12,13). A summary of the included studies and baseline characteristics of the participants is provided in

Table (1) compares four clinical trials studies investigating Lebrikizumab for atopic dermatitis (AD), including studies by Guttman-Yassky (2020),Simpson (2023), and Silverberg (2023, ADVocate 1 and 2). Participants across all studies had similar severity of AD (measured by EASI scores) and included different racial groups with various compositions. In all studies, Lebrikizumab was administered in doses of 250mg every two or four weeks, with an initial loading dose and the treatment duration ranges between 16 and 52 weeks. Across the studies, Lebrikizumab showed significant improvements in skin clearance, decreasing in AD severity, and enhanced quality of life, with notable reductions in itching and better sleep. These findings were observed across different racial groups, indicating the broad efficacy of Lebrikizumab in AD treatment.

Risk of Bias Assessment

By using the Cochrane risk of bias tool of RCT two reviewers did the risk of bias assessment independently reviewed and rated if the study was high risk or not, all trials were low risk of bias. Figure 2 & figure 3

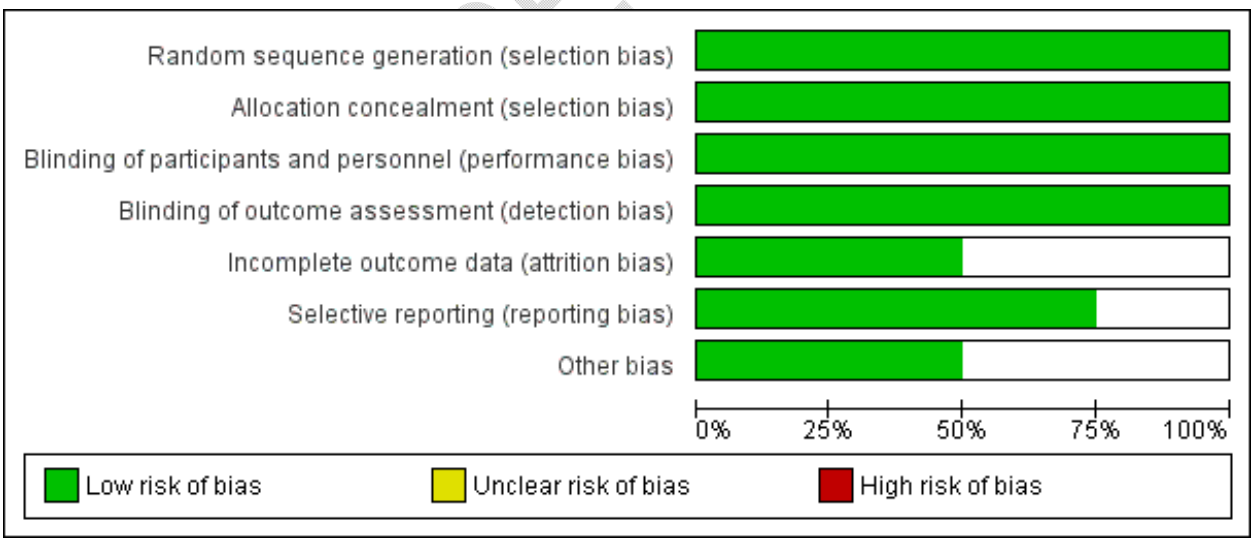

Figure 2 Risk of bias graph

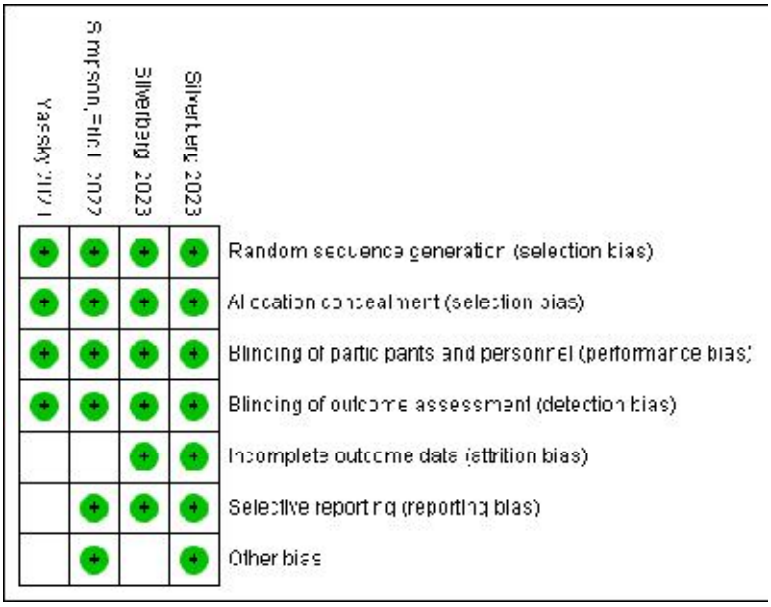

Figure 3: Risk Of Bias graph

This graph assesses the "Risk of bias" in each of the following studies (Silverberg 2023, Silverberg 2023, Simpson, Eric L 2022, yassky 2020). The green "+" symbol means a low risk of bias. In summary, the figure concludes that all the studies reviewed had a low risk of bias across all of the proposed domains.

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Change in Eczema Area and Severity Index (EASI)

The total analysis demonstrated a statistically significant improvement in the Change of EASI with lebrikizumab compared to placebo (mean difference (MD): -25.60, 95% CI [-38.01, -13.18], P < 0.0001) (Figure 4). Lebrikizumab at 250mg Q2W showed a statistically significant improvement in the Change of EASI compared to placebo (MD: -34.86, 95% CI [-41.45, -28.27], P < 0.00001). Pooled studies showed no heterogeneity (P = 0.63; I^2 = 0%).

Lebrikizumab at 250mg Q4W showed a statistically significant improvement in the Change of EASI compared to placebo (MD: -28.09, 95% CI [-46.31, -9.87], P = 0.003).

Lebrikizumab at 125mg Q4W showed no significant difference between the two groups (MD: -10.41, 95% CI [-28.31, 7.48], P = 0.25). Pooled studies demonstrated heterogeneity (P = 0.09; I^2 = 66%).

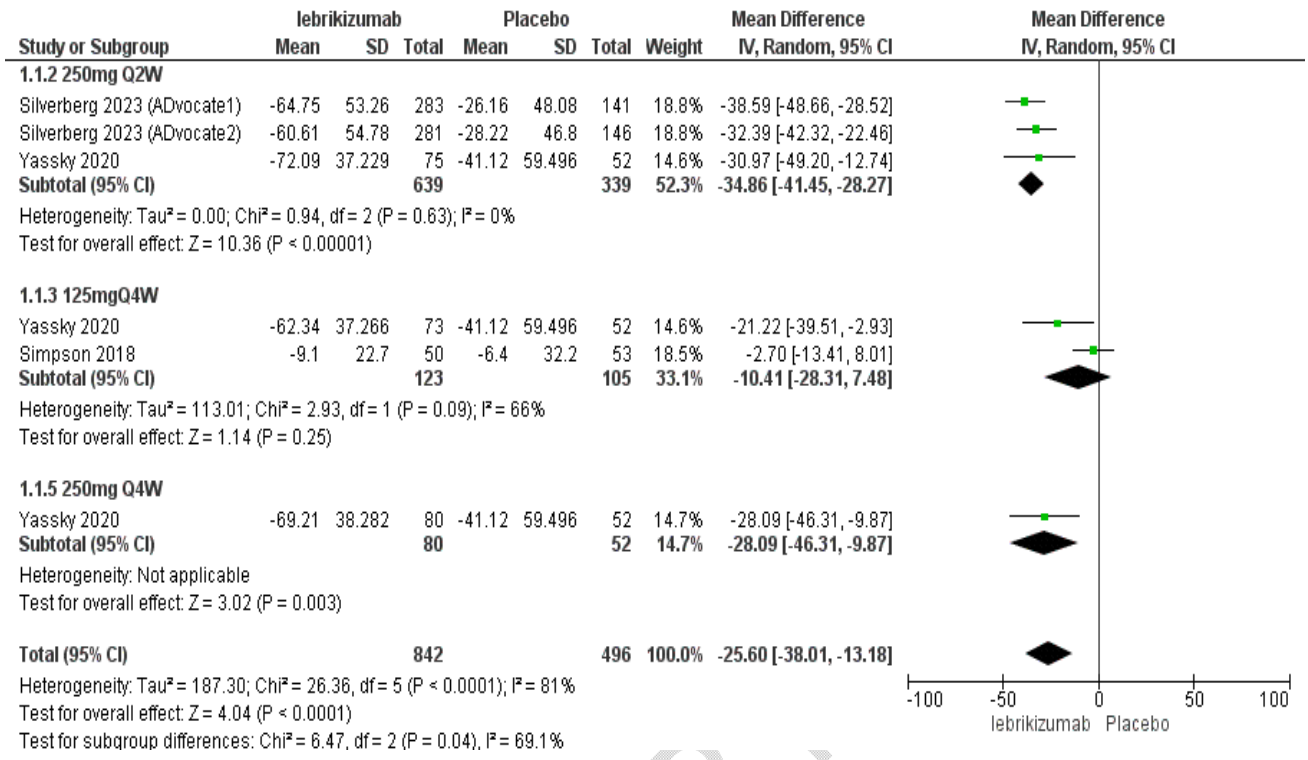

Figure 4 Change in EASI

This figure focuses on the changes in EASI (Eczema Area and Severity Index). It compares lebrikizumab to a placebo group. Overall, the figure demonstrates that across various studies, lebrikizumab shows more significant reduction in eczema severity compared to placebo, with a statistically significant overall result. The high heterogeneity (81%) suggests that the studies are to a certain degree variable in their effect sizes, but the treatment is generally effective.

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Change in body surface area (BSA)

The total analysis demonstrated a statistically significant improvement in the Change of BSA with lebrikizumab compared to placebo (MD: -9.81, 95% CI [-15.39, -4.23], P < 0.0006) (Figure 5). Lebrikizumab at 250mg Q2W showed a statistically significant improvement in the Change of BSA compared to placebo(MD: -14.74 , 95% CI[-19.82, -9.65], P < 0.00001).Pooled studies demonstrated heterogeneity (P = 0.02; I^2 = 74%), A sensitivity analysis was conducted, and the heterogeneity was best resolved by excluding the yassky 2020 study (I^2 =0%, P =0.32) (Figure 6). Lebrikizumab at 250mg Q4W showed a statistically significant improvement in the Change of BSA compared to placebo (MD: -7.50 , 95% CI [-14.61, -0.39], P = 0.04). Lebrikizumab at 125mg Q4W showed no significant difference between the two groups (MD:-

2.51 , 95% CI [-8.25, 3.23], P = 0.39). Pooled studies showed no heterogeneity (P = 0.88; I^2 = 0%).

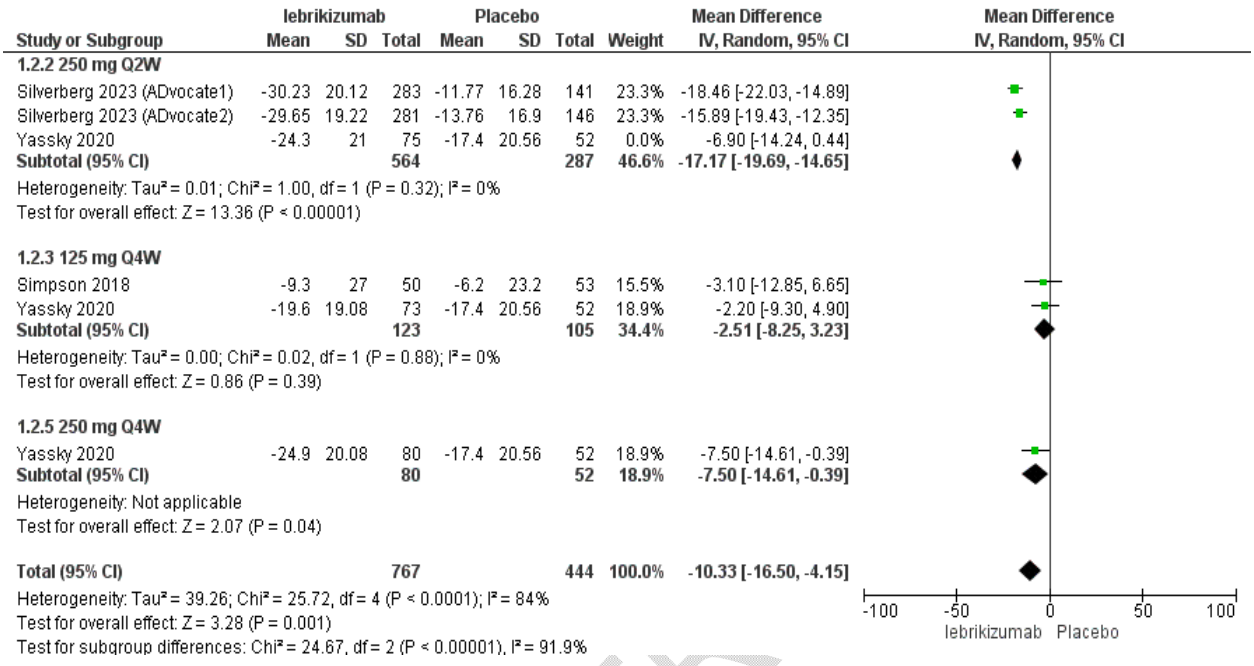

Figure 5: Changes in BSA (Body Surface Area) are shown in this figure. Lebrikizumab revealed a statistically significant decrease in BSA compared to placebo. However, there is considerable heterogeneity between the studies, especially for different dosages and intervals.

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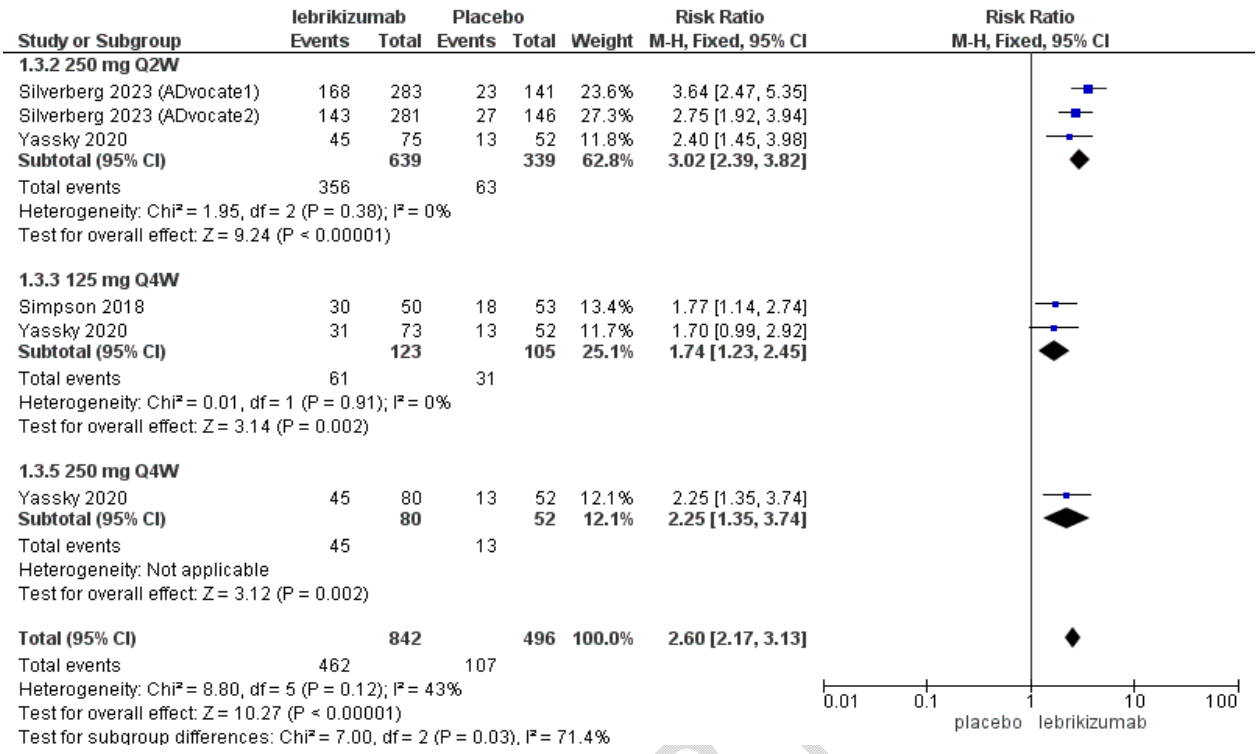

Figure 6 Leave-one meta-analysis of change in BSA

In this figure, the total number of events and studies included in the analysis is summarised, providing an overall risk ratio of 2.60. This indicates a significantly increased risk of the outcome associated with lebrikizumab compared to placebo.

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Eczema Area and Severity Index (EASI 75) score

The total analysis demonstrated a statistically significant improvement in the EASI 75 score with lebrikizumab compared to placebo (Risk Ratio (RR):2.60, 95% CI [2.17, 3.13], P < 0.00001) (Figure 7).

Lebrikizumab at 250mg Q2W showed a statistically significant improvement in the EASI 75 score compared to placebo(RR: 3.02 , 95% CI [2.39, 3.82], P < 0.00001).Pooled studies showed no heterogeneity (P = 0.38; I^2 = 0%).

Lebrikizumab at 250mg Q4W showed a statistically significant improvement in the EASI 75 score compared to placebo (RR: 2.25 , 95% CI [1.35, 3.74], P < 0.002).

Lebrikizumab at 125mg Q4W showed a statistically significant improvement in the EASI 75 score compared to placebo (RR: 1.74 , 95% CI [1.23, 2.45], P < 0.002) .Pooled studies showed no heterogeneity (P = 0.91; I^2 = 0%).

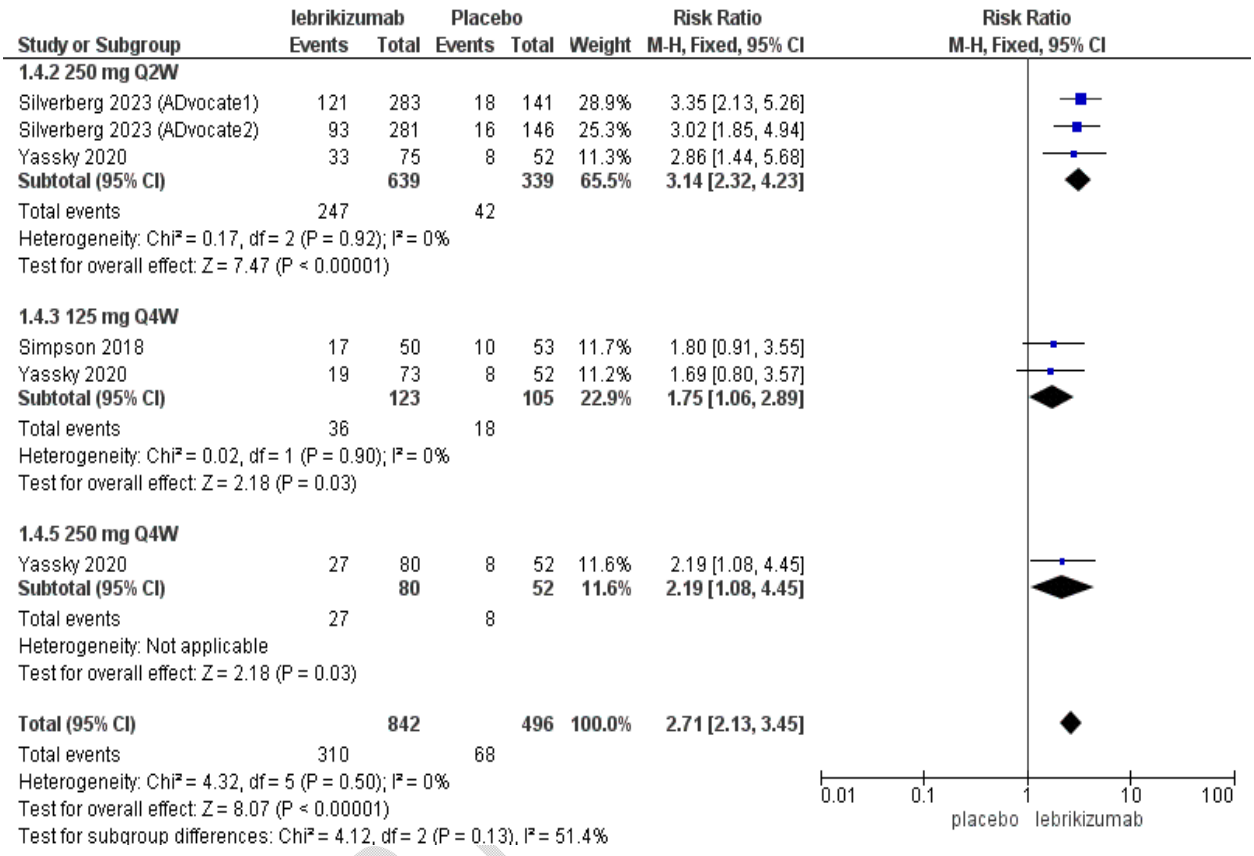

Figure 7 EASI 75 score

In this figure, the forest plot visually represents each study's risk ratio and confidence intervals with squares (point estimates) and horizontal lines (CIs). The diamond at the bottom displays the overall effect estimate. This analysis shows that lebrikizumab has a statistically significant effect compared to placebo across various studies, with risk ratios showing favourable results for lebrikizumab.

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Investigator's Global Assessment (IGA) score

The total analysis demonstrated a statistically significant improvement in the IGA score with lebrikizumab compared to placebo ((RR:2.71, 95% CI [2.13, 3.45], P < 0.00001) (Figure 8).

Lebrikizumab at 250mg Q2W showed a statistically significant improvement in the IGA score compared to placebo (RR: 3.14, 95% CI [2.32, 4.23], P < 0.00001). Pooled studies showed no heterogeneity (P = 0.92; I^2 = 0%).

Lebrikizumab at 250mg Q4W showed a statistically significant improvement in the IGA score compared to placebo (RR: 2.19, 95% CI [1.08, 4.45], P < 0.03).

Lebrikizumab at 125mg Q4W showed a statistically significant improvement in the IGA score compared to placebo (RR: 1.75, 95% CI [1.06, 2.89], P < 0.03). Pooled studies showed no heterogeneity (P = 0.90; I^2 = 0%).

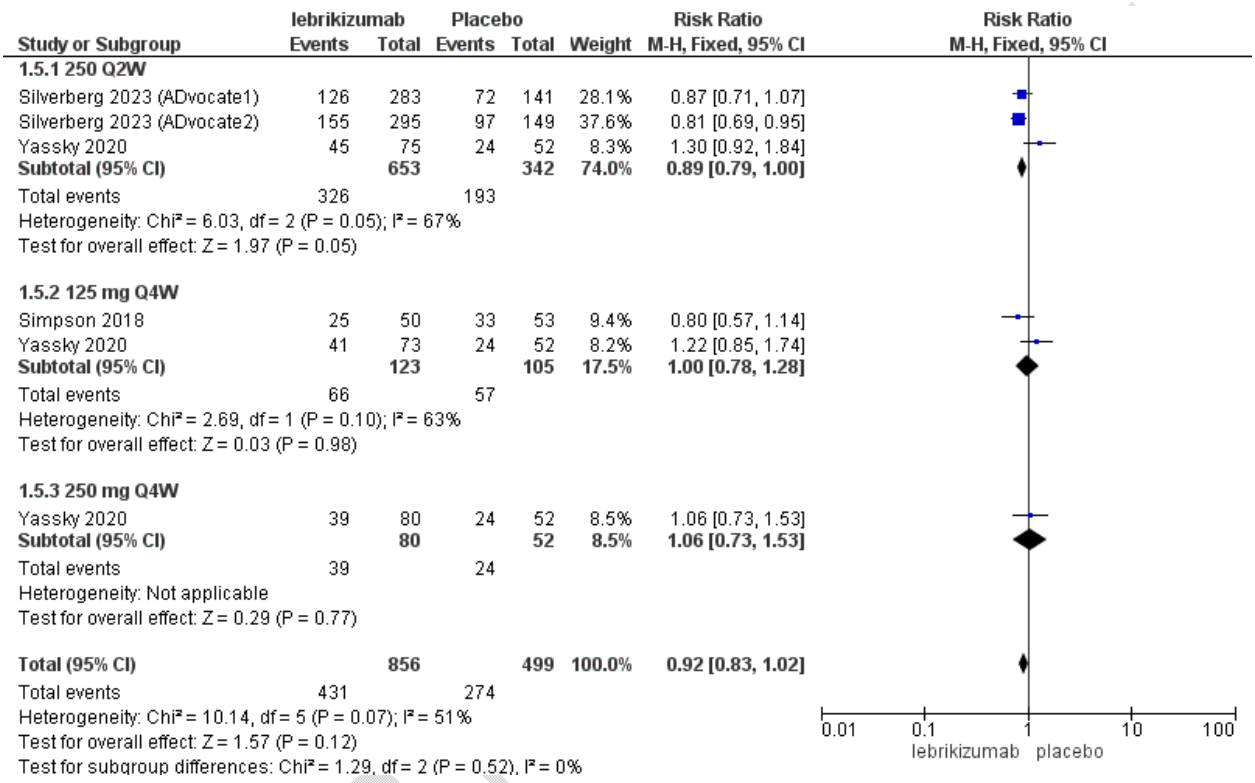

Figure 8 IGA score are shown in this figure , This figure show that lebrikizumab at different doses doesn't significantly improve Investigator's Global Assessment (IGA) scores compared to placebo. The combined result shows minimal improvement, but it is not statistically significant across most doses.

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Non-serious adverse events (NSAEs)

The total analysis demonstrated no statistical difference in the incidence of NSAEs with lebrikizumab compared to placebo (RR:0.92, 95% CI [0.83, 1.02], P =0.12) (Figure 9).

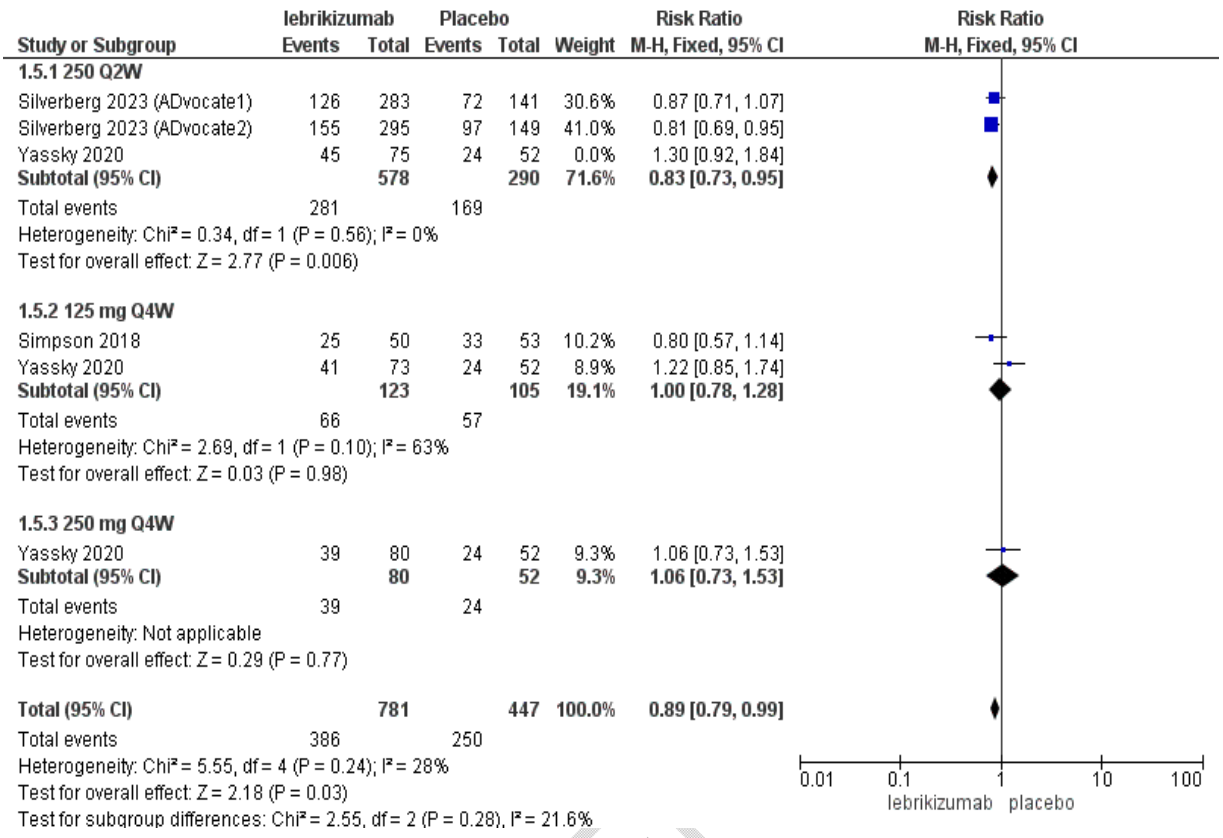

Figure 9 non-serious adverse events (NSAEs) . this figure shows that lebrikizumab at 250 mg every 2 weeks is associated with a small reduction in non-serious adverse events compared to placebo, while other doses show no significant difference. Overall, lebrikizumab slightly reduces NSAEs.

Lebrikizumab at 250mg Q2W showed no statistical difference in the incidence of NSAEs compared to placebo (RR: 0.89, 95% CI [0.79, 1.00], P=0.05). Pooled studies showed heterogeneity (P = 0.05; I^2 = 67%). A sensitivity analysis was conducted, and the heterogeneity was best resolved by excluding the yassky 2020 study (I^2 =0%, P =0.56) (Figure 10).

Lebrikizumab at 250mg Q4W showed no statistical difference in the incidence of NSAEs compared to placebo (RR: 1.06, 95% CI [0.73, 1.53], P < 0.77). Lebrikizumab at 125mg Q4W showed no statistical difference in the incidence of NSAEs compared to placebo (RR: 1.00, 95% CI [0.78, 1.28], P = 0.98). Pooled studies showed heterogeneity (P = 0.10; I^2 = 63%).

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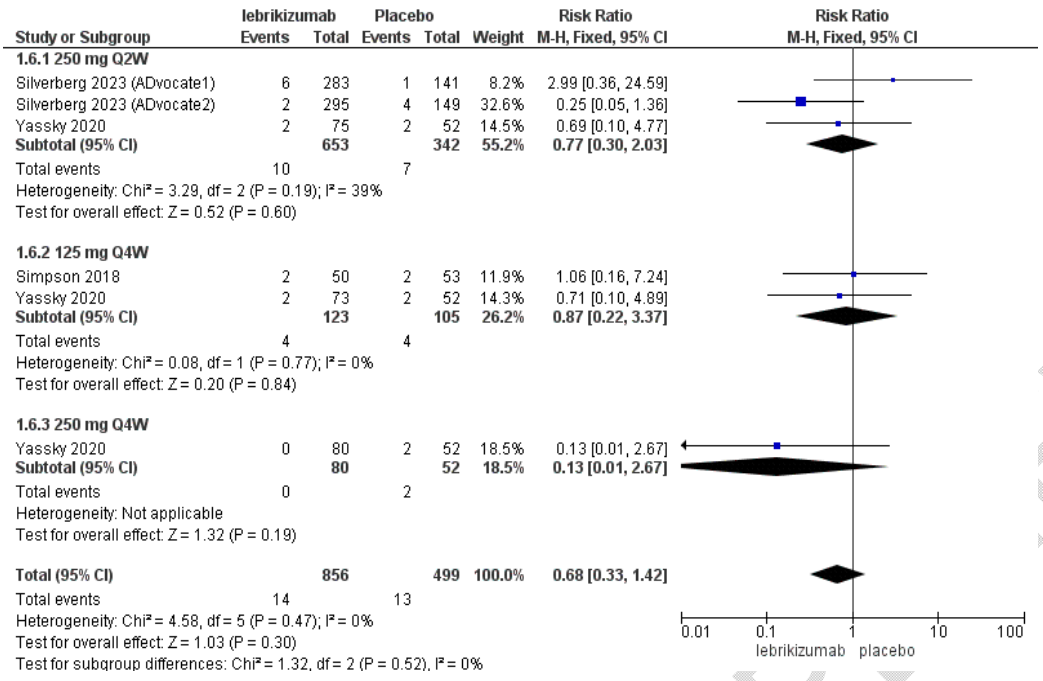

Figure 10 leave-one meta-analysis of NSAEs . This figure shows the effects of removing one study at a time to test the stability of results on NSAEs. The overall outcome remains similar, confirming the robustness of findings that lebrikizumab slightly reduces NSAEs without substantial variation.

Serious adverse events (SAEs)

The total analysis demonstrated no statistical difference in the incidence of SAEs with lebrikizumab compared to placebo (RR:0.68, 95% CI [0.33, 1.42], P =0.30) (Figure 11).

Lebrikizumab at 250mg Q2W showed no statistical difference in the incidence of SAEs compared to placebo (RR:0.77, 95% CI [0.30, 2.03], P=0.60). Pooled studies showed no heterogeneity (P = 0.19; I^2 = 39%).

Lebrikizumab at 250mg Q4W showed no statistical difference in the incidence of SAEs compared to placebo (RR: 0.13, 95% CI [0.01, 2.67], P < 0.19). Lebrikizumab at 125mg Q4W showed no statistical difference in the incidence of SAEs compared to placebo (RR: 0.87, 95% CI [0.22, 3.37], P = 0.84). Pooled studies showed no heterogeneity (P =0.77; I^2 = 0%).

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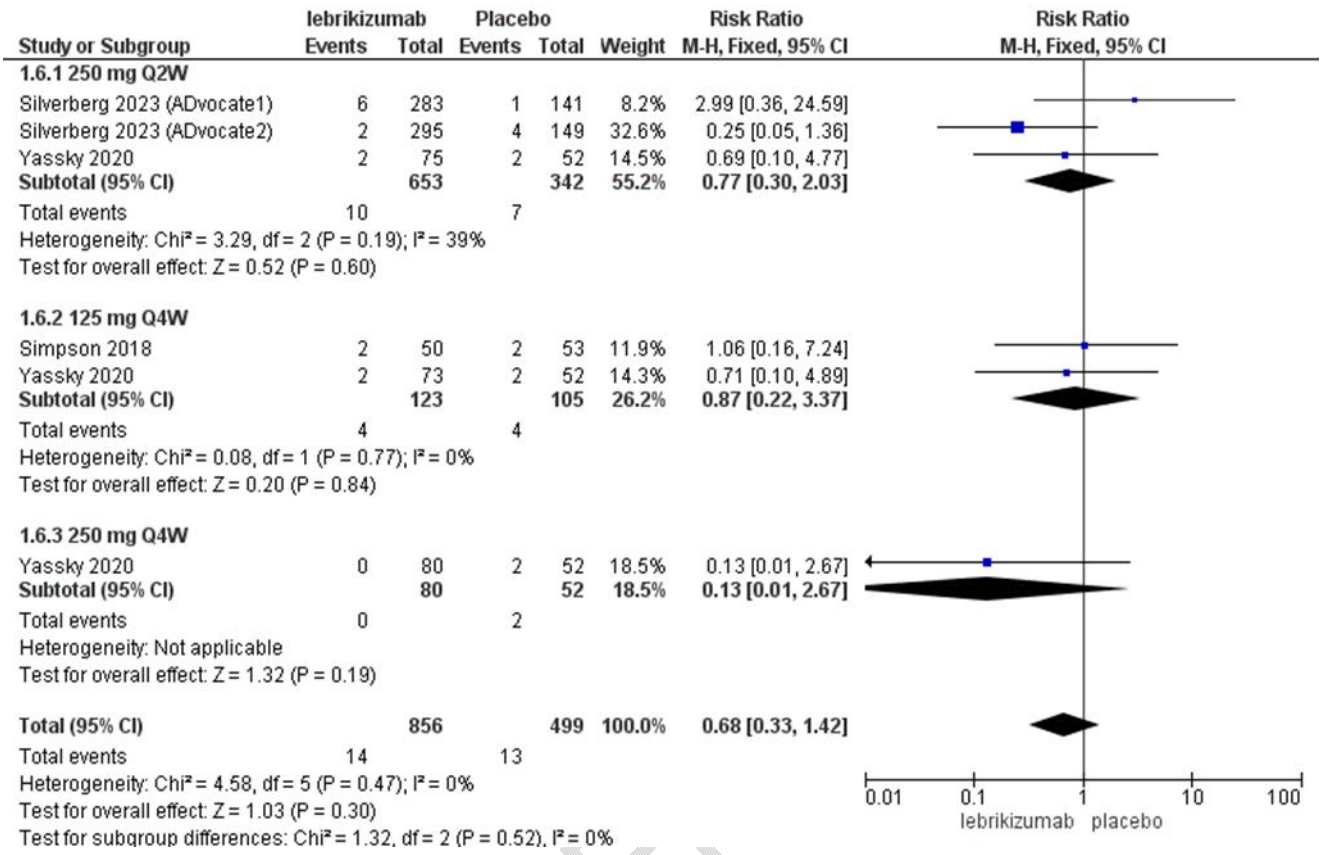

Figure 11 Serious adverse events (SAEs). This figure shows lebrikizumab doesn't significantly increase serious adverse events compared to placebo in all doses, indicating its safety concerning serious side effects. The pooled result indicates no significant difference between lebrikizumab and placebo for SAEs.

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Discussion

Atopic dermatitis presents with diverse signs and symptoms, influenced by many factors such as age, ethnicity, and socioeconomic status (14). Pruritus, the most reported symptom among patients with AD is predominantly mediated by cytokines, such as interleukin-13 (IL-13) via stimulation of peripheral sensory neurons, rather than histamine-driven mechanisms(15). IL-13 has also been implicated in the impairment of epidermal barrier function, skin thickening, and recruitment of inflammatory cells (15,16). This targeted approach may provide advantages over broader treatments and support key treatment goals for AD, such as reducing inflammation, preserving skin barrier function, alleviating dryness and pruritus, and preventing infections and flare-ups. Although corticosteroids remain the first-line therapy for moderate-to-severe AD, concerns about adverse effects and patients' fears about using these medications, which may affect their compliance, underscore the demand for new therapeutic options(17–19). The first IL-

13 inhibitor to receive FDA approval is Tralokinumab, whichis effective and safe in treating AD(20,21).

This review paper was done using different databases and tools, for example, Clinical Trials, Ovid, ScienceDirect, Google Scholar, and PubMed to find as many qualified studies as possible and to narrow down the spectrum of studies used to only the studies that meet the detailed criteria that the study researchers set for this paper by using Cochrane, this process has made this review study more depersonalized of the researchers' biases which made the results more reliable. Due to the methods mentioned above for the selection criteria and the novelty of Lebrikizumab, it was challenging to find a lot of studies due to the low number of RCTs.

In this systematic review and meta-analysis, four clinical trials with a cumulative sample size of 1,686 patients were enrolled to evaluate the efficacy and safety of lebrikizumab as a monotherapy for the management of atopic dermatitis. We found that treatment with lebrikizumab, compared to a placebo, significantly improves all the evaluated parameters of moderate to severe AD, including Eczema Area and Severity Index (EASI), Body Surface Area (BSA), EASI 75 (representing a 75% improvement in EASI), and Investigator's Global Assessment (IGA) scores. These findings underscore the therapeutic promise of IL-13 inhibition in reducing disease activity and enhancing patient outcomes in AD management. Regarding safety, we found that there is no difference in the incidence of serious adverse events (SAEs) and non-serious adverse events (NSAEs) between the placebo group and the treatment group receiving lebrikizumab. By addressing inflammation at its source, this targeted approach has the potential to improve treatment outcomes while minimizing the risks associated with non-specific therapies.

Study limitations encompassed the exclusion of pediatric age groups, focusing instead on the young and elderly cohorts. For instance, in [Eric L. Simpson], the trial enrolled 211 participants with moderate to severe AD aged ≥12 to <18, spanning a 16-week duration. Conversely, [Jonathan I. Silverberg] followed a group aged 12 to >18 for 52 weeks, highlighting the potential age-dependent effects of Lebrikizumab. Additionally, the short treatment duration, typically lasting a few months in both placebo and treatment arms, such as in [Emma Gutman-Yassky] (16 weeks), may preclude the comprehensive evaluation of long-term efficacy and safety, as observed in [Eric L. Simpson] (52 weeks). Despite these limitations, efforts were made to mitigate biases and ensure the study's accuracy.

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Another key limitation is the heterogeneity observed in certain pooled results, particularly for adverse events. While sensitivity analyses mitigated some of this heterogeneity, they point to variations in trial design and patient populations that may impact the consistency of the findings.

In summary of the aforementioned points, lebrikizumab has demonstrated promise as a treatment option for AD. It has shown significant effectiveness across various measures and has exhibited a favorable safety profile. However, there is a need for real-world experience studies and additional trials to evaluate lebrikizumab in comparison to other treatment options as well as evaluating it for long-term safety and efficacy.

Conclusion

Amongst 227 articles, four studies met the criteria for evaluating lebrikizumab's efficacy and safety in treating atopic dermatitis (AD). The analysis of 1,686 patients provided evidence supporting lebrikizumab’s efficacy in improving both EASI and IGA scores compared to placebo. Notably, lebrikizumab achieved significant results in the EASI 75 response rate, demonstrating clinically meaningful improvement. Regarding safety, there was no significant difference in the incidence of non-serious adverse events (NSAEs) or serious adverse events (SAEs) between lebrikizumab and placebo, reinforcing its favorable safety profile. This finding highlights that although lebrikizumab shows potential, its therapeutic benefit may be limited in some cases.

Study Limitations and Future Directions

This review has some limitations, including the exclusion of children and the relatively short treatment periods in most trials, which could limit how broadly the results apply, especially for long-term use. While these studies indicate that lebrikizumab has potential in treating AD, future research should focus on real-world applications, comparisons with other AD treatments, and longer-term evaluations of both safety and effectiveness. Fine-tuning dosage and treatment protocols could further improve results while reducing side effects.

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Table 1: Comparative list of four clinical trials investigating Lebrikizumab for atopic dermatitis

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Study name	year	Clinical identifier	Control group			Treatment group				Treatment dosage / frequency	duration	results
			No. of participa male	severity of AD (EASI) Mean (SD)	Race (%)	No. of participa male	severity of AD (EASI) Mean (SD)	Race (%)	age			
Simpson, Eric L./ 2023	2023	NCT04250337	66/33	26.4 (10.6)	Asian(19.7), Black/African American(13.6), White(60.6)	145/75	27.7 (11.1)	Asian(12.4), Black/African American(13.1), White(62.1)	19.9	Loading dose 500mg week 0 250mg /every two weeks 16 week	16 week	The study showed that lebrikizumab combined with topical corticosteroids (TCS) significantly improved skin clearance in patients with atopic dermatitis .and 75% improvement in the Eczema Area and Severity Index (EASI-75). The treatment also led to improvements in secondary endpoints and most adverse events were mild or moderate.
Silverberg 2023 (ADvocate1)	2023	NCT04146363	141/68	31(12.9)	White (66), Asian (22), Black (11.3)	283/142	28.8(11.3)	White (69.3), Asian (13.8), Black (11.7),	36.1	Loading does 500mg week 0 250mg /every two weeks	52 week	Lebrikizumab therapy showed significant improvements in primary and secondary outcomes, including skin clearance, itch, and sleep disturbance, as early as week 2. It demonstrated a rapid onset of action in various aspects of atopic dermatitis.
Silverberg 2023 (ADvocate2)	2023	NCT04178967	146/71	29.6 (10.8)	White (58.2), Asian (30.1), Black (6.8), Other (4.8)	281/145	29.7 (12)	White (59.8), Asian (27.8), Black (8.9), Other (3.6)	36.6	Loading does 500mg week 0 250mg /every two weeks	52 week	Lebrikizumab therapy demonstrated significant improvements in skin clearance, itch, and sleep interference compared to placebo at week 16, indicating rapid effectiveness in treating multiple aspects of the disease.
Emma Guttman-Yassky / 2020	2020	NCT03443024	52/28	28.9(11.8)	White (50.0), Black or African American(30.8), American Indian or Alaskan native(0), Asian(11.5), other(7.7)	73/27	29.9(13.5)	White(50.7), Black or African American(35.6), American Indian or Alaskan native(1.4), Asian(11.0), other(1.4)	16.5	Loading dose 250mg week 0 125mg /every four weeks	16 week	The primary endpoint was the percentage change in Eczema Area and Severity Index (EASI) from baseline to week 16. Secondary endpoints included various improvements in EASI, Investigator's Global Assessment, and pruritus numeric rating scale scores, as well as monitoring of treatment-emergent adverse events.
						80/33	26.2 (10.1)	White(52.5), Black or African American(35.0), American Indian or Alaskan native(1.3), Asian(8.8), other(2.5)	17.9	Loading dose 500mg week 0 250mg /every four weeks		
						75/26	25.5 (11.2)	White(53.3), Black or African American(30.7), American Indian or Alaskan native(1.3), Asian(8.0), other(6.7)	17.4	Loading dose 500mg week 0 250mg /every two weeks		

study ID	lebrikizumab		placebo					
	mean	SD	mean	SD	mean	SD		
Silverberg 2023 (ADvocate1)	-30.23	20.12	--	--	--	--	-11.77	16.28
Silverberg 2023 (ADvocate2)	-29.65	19.22	--	--	--	--	-13.76	16.9
Simpson 2018	--	--	-9.3	27	--	--	-6.2	23.2
Yassky 2020	-24.3	21	-19.6	19.08	-24.9	20.08	-17.4	20.56

Table 2 The summary of included studies, change in Eczema Area and Severity (EASI)

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	Change in Eczema Area and Severity Index (EASI)								
	250mg Q2W		125mgQ4W		250mg Q4W		mean	SD	
	mean	SD	mean	SD	mean	SD			
Silverberg 2023 (ADvocate1)	-64.75	53.26	--	--	--	--	-26.16	48.08	
Silverberg 2023 (ADvocate2)	-60.61	54.78	--	--	--	--	-28.22	46.8	
Simpson 2018	--	--	-9.1	22.7	--	--	-6.4	32.2	
Yassky 2020	-72.09	37.229	-62.34	37.266	-69.21	38.282	-41.12	59.496	

Table 3 The summary of included studies, Change in Body Surface Area (BSA)

study ID	lebrikizumab						placebo	
	Eczema Area and Severity Index (EASI75I) score							
	250mg Q2W		125mgQ4W		250mg Q4W		event	total
	event	total	event	total	event	total		
Silverberg 2023 (ADvocate1)	168	283	--	--	--	--	23	141
Silverberg 2023 (ADvocate2)	143	281	--	--	--	--	27	146
Simpson 2018	--	--	30	50	--	--	18	53
Yassky 2020	45	75	31	73	45	80	13	52

Table 4 The summary of included studies,Eczema Area and Severity Inde (EEASI75I) score

study ID	lebrikizumab						placebo	
	Investigator's Global Assessment (IGA) score							
	250mg Q2W		125mgQ4W		250mg Q4W		event	total
	event	total	event	total	event	total		
Silverberg 2023 (ADvocate1)	121	283	--	--	--	--	18	141
Silverberg 2023 (ADvocate2)	93	281	--	--	--	--	16	146
Simpson 2018	--	--	17	50	--	--	10	53
Yassky 2020	33	75	19	73	27	80	8	52

Table 5 The summary of included studies, Investigaters Global Assessment (IGA)

study ID	lebrikizumab						placebo	
	non-serious adverse events (NSAEs)							
	250mg Q2W		125mgQ4W		250mg Q4W		event	total
	event	total	event	total	event	total		
Silverberg 2023 (ADvocate1)	126	283	--	--	--	--	72	141
Silverberg 2023 (ADvocate2)	155	295	--	--	--	--	97	149
Simpson 2018	--	--	25	50	--	--	33	53
Yassky 2020	45	75	41	73	39	80	24	52

Table 6The summary of included studies, non-serious adverse events (NSAEs)

study ID	lebrikizumab						placebo		
	serious adverse events (SAEs)								
	250mg Q2W		125mgQ4W		250mg Q4W		event	total	
	event	total	event	total	event	total			
Silverberg 2023 (ADvocate1)	6	283	--	--	--	--	1	141	
Silverberg 2023 (ADvocate2)	2	295	--	--	--	--	4	149	
Simpson 2018	--	--	2	50	--	--	2	53	
Yassky 2020	2	75	2	73	0	80	2	52	

Table 7 The summary of included studies, serious adverse events (SAEs)

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