Review Article

Efficacy and Safety of Deucravacitinib for The Treatment of Chronic Plaque Psoriasis: A Systematic Review and Meta-Analysis

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Abstract

Background: Deucravacitinib, an oral selective tyrosine kinase 2 (TYK2) inhibitor, represents a novel therapeutic class for moderate-to-severe plaque psoriasis. This systematic review and meta-analysis evaluates its efficacy and safety. The objective is to evaluate the efficacy and safety of deucravacitinib compared to placebo and active controls (e.g., apremilast) in patients with moderate-to-severe chronic plaque psoriasis. **Material and Methods:** We systematically searched PubMed, Embase, Cochrane Central Register of Controlled Trials, and ClinicalTrials.gov from inception to December 2023 for randomized controlled trials (RCTs). Primary outcomes were the proportion of patients achieving ≥75% improvement in Psoriasis Area and Severity Index (PASI 75) and a static Physician's Global Assessment (sPGA) score of 0/1 at Week 16. Safety outcomes included adverse events. Data were pooled using a random-effects model. **Results:** Eight RCTs (N=5,243 patients) were included. Deucravacitinib was significantly superior to placebo and apremilast. The risk ratio (RR) for achieving PASI 75 vs. placebo was 4.59 (95% CI: 3.82–5.51; p<0.001) and vs. apremilast was 1.66 (95% CI: 1.42–1.95; p<0.001). PASI 90 and PASI 100 responses were also significantly higher. The incidence of serious adverse events was low (<2%) and comparable to placebo. Deucravacitinib had a lower incidence of gastrointestinal events than apremilast. **Conclusion:** Deucravacitinib is an effective and well-tolerated oral treatment for moderate-to-severe plaque psoriasis, demonstrating superior efficacy to apremilast and a favorable safety profile. It presents a valuable therapeutic option, particularly for patients seeking an effective oral therapy.

Keywords: Psoriasis; Deucravacitinib; Tyrosine Kinase 2 (TYK2) inhibitor; Systematic review, Efficacy; Safety.

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Introduction

Psoriasis is an immune-mediated, chronic inflammatory disease that primarily affects the skin and joints, significantly impacting a patient's physical health, mental well-being, and overall quality of life (QoL). It is associated with a persistent dysregulation of the immune system, leading to hyperproliferation of keratinocytes and chronic inflammation. Beyond its dermatological manifestations, psoriasis is now recognized as a systemic disease with an increased risk of multiple comorbidities, including cardiovascular disease, metabolic syndrome, type 2 diabetes mellitus, anxiety, depression, and an elevated risk of all-cause mortality.[1,2] Additionally, psoriatic patients often experience fatigue, social stigma, and work-related impairment, further reducing their quality of life (QoL).[3]

Clinically, psoriasis is characterized by large, erythematous, scaly plaques that most commonly appear on the scalp, trunk, and extensor surfaces such as the elbows and knees. The severity and distribution of these plaques vary among individuals and may fluctuate over time due to genetic, environmental, and immunological factors.[4] The underlying pathology of psoriasis is driven by an intricate immune response, primarily involving the IL-23/IL-17 signaling axis, which promotes sustained inflammation and keratinocyte hyperproliferation.[5] Despite significant advances in understanding its pathophysiology, psoriasis remains incompletely understood, and ongoing research continues to refine therapeutic strategies.

For moderate psoriasis, topical treatments such as glucocorticosteroids, vitamin D analogs, or their combinations are generally effective. In delicate areas such as the face and intertriginous regions, topical calcineurin inhibitors (TCIs) like tacrolimus and pimecrolimus are often used due to their lower risk of skin atrophy compared to corticosteroids.[6]

For more severe cases, systemic therapies are employed. Traditional systemic treatments include methotrexate, ciclosporin, acitretin, and fumaric acid esters. However, long-term use of these agents requires careful monitoring due to the risk of cumulative organ toxicity and drug-drug interactions. Among them, cyclosporin A is typically used for short-term flare

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control, while the others can be employed for long-term disease maintenance with appropriate monitoring.[2] Additionally, apremilast, an oral phosphodiesterase-4 (PDE4) inhibitor, has been approved for use in both the United States and Europe, offering a non-biologic systemic option with a favorable safety profile.[7]

Biologic therapies have revolutionized the treatment of psoriasis by specifically targeting inflammatory pathways, with commonly used agents including tumor necrosis factor-alpha (TNF-α) inhibitors such as etanercept, adalimumab, certolizumab, and infliximab; IL-23 inhibitors that target the p19 subunit such as guselkumab, tildrakizumab, risankizumab, and mirikizumab; IL-17 inhibitors such as secukinumab, ixekizumab, bimekizumab, and brodalumab; and IL-12/IL-23 inhibitors that target the p40 subunit, such as ustekinumab.

These biologics are also approved for the treatment of psoriatic arthritis, reflecting their effectiveness in both skin and joint manifestations of the disease.[8]

A newer oral therapy, deucravacitinib, is a selective tyrosine kinase 2 (TYK2) inhibitor currently under investigation for multiple autoimmune diseases, including lupus, ulcerative colitis, psoriatic arthritis, moderate-to-severe plaque psoriasis, and Crohn's disease. Unlike traditional TYK2 or Janus kinase (JAK) inhibitors, which bind to the active catalytic domain, deucravacitinib binds to a unique regulatory domain pocket, allowing for highly selective allosteric inhibition of TYK2. This selectivity minimizes off-target effects and enhances safety, making it a promising alternative in psoriasis treatment.[9]

The objective of this research study is to evaluate the clinical efficacy and quality-of-life (QoL) outcomes associated with deucravacitinib in patients with psoriasis and to analyze its effectiveness in comparison to findings from other studies.

Pharmacotherapy of Psoriasis

1. Current Treatment Options and Challenges

Psoriasis treatment involves a combination of topical therapies, phototherapy, and systemic medications, depending on disease severity. For patients with psoriatic arthritis (PsA), a range of pharmacological options—including nonsteroidal anti-inflammatory drugs (NSAIDs), disease-modifying antirheumatic drugs (DMARDs), and biologic agents—have demonstrated variable efficacy in controlling both joint and skin manifestations.[10]

Traditional systemic treatments, such as methotrexate and cyclosporine, have been widely used due to their immunosuppressive properties. These agents can lead to dramatic improvements in psoriatic skin lesions, though their long-term use is limited by potential toxicities and the need for regular monitoring.[11]

In recent years, oral Janus kinase (JAK) inhibitors have emerged as a novel class of systemic therapy for psoriasis and psoriatic arthritis. JAK inhibitors work by reducing proinflammatory cytokine signalling and production, effectively blocking multiple cytokines involved in psoriasis pathogenesis, including interleukin (IL)-2, IL-4, IL-6, IL-7, IL-9, IL-12, IL-15, IL-17, IL-21, and IL-23.[12] These small-molecule inhibitors offer a more targeted yet broad-spectrum approach to controlling inflammation compared to traditional immunosuppressive drugs.

2. Drawbacks and Limitations of Current Therapies

Addressing Limitations of Current Psoriasis Therapies: Current psoriasis treatments face several challenges, including long-term organ toxicity, increased risks of infections and malignancies, and significant drug–drug interactions. These limitations have driven the search for safer and more effective therapeutic strategies. Deuteration—a novel approach involving the substitution of hydrogen atoms with deuterium—offers a promising solution by enhancing drug selectivity, reducing side effects, and improving metabolic stability.

Safety Concerns with JAK Inhibitors: JAK inhibitors, such as tofacitinib, have emerged as effective oral treatments targeting cytokine-mediated inflammation in psoriasis. However, their use has been associated with several adverse effects. One of the primary concerns is lipid-related alterations, as tofacitinib treatment has been linked to changes in lipid parameters, which may potentially increase the risk of atherosclerosis.[13] Additionally, although large-scale cardiovascular risks are not frequently reported, studies suggest a possible link between JAK inhibition and a higher incidence of major adverse cardiovascular events (MACE).[14]

Need for Safer, Targeted Alternatives: Deuteration, a chemical modification that replaces hydrogen atoms with deuterium, has emerged as a promising approach to improving drug safety and specificity. Unlike traditional JAK inhibitors, deuterated compounds retain JAK kinase activity while selectively targeting specific tyrosine kinases, thereby reducing broad immune suppression. Additionally, they have demonstrated a lower incidence of adverse effects, which may enhance patient adherence and improve long-term treatment outcomes.[11] While JAK inhibitors provide a valuable oral alternative for psoriasis treatment, their cardiovascular risks, lipid-related effects, and adverse event profile limit their widespread use. Deuteration offers a promising alternative by enhancing drug safety and selectivity, though further clinical studies are needed to confirm its long-term efficacy.

The Role of Deuteration in Psoriasis Therapy

3. Introduction to Deuteration

What is Deuteration?: Deuteration is a form of bioisosterism, a technique in medicinal chemistry where one substructure of a compound is replaced with another to enhance specific properties while maintaining biological activity.[11] In this context, hydrogen (H) is substituted with deuterium (D), a stable isotope of hydrogen, which has significant effects on drug metabolism and pharmacokinetics.

Impact of Deuteration on Drug Properties: Initially, deuteration was primarily utilized to increase the metabolic stability of drugs by reducing the rate of enzymatic degradation, particularly through cytochrome P450-mediated oxidation [15]. However, recent studies indicate that deuterium incorporation not only enhances pharmacokinetic (PK) properties but also modifies drug efficacy and safety, leading to improved therapeutic outcomes[16].The substitution of hydrogen with deuterium is one of the most conservative and well-established bioisosteric modifications. Although deuterium shares many chemical properties with hydrogen, it differs in several important aspects. Firstly, deuterium has twice the mass of hydrogen, which significantly influences molecular vibrations and enhances bond

stability. Secondly, the carbon-deuterium (C–D) bond is stronger than the carbon-hydrogen (C–H) bond, with a bond energy difference of 1.2–1.5 kcal/mol, making it more resistant to metabolic cleavage.[17] Additionally, due to its heavier mass, deuterium exhibits a reduced vibrational stretching frequency, which results in slower bond cleavage and an extended drug half-life.[18] Finally, deuteration can subtly influence pharmacokinetic properties by reducing lipophilicity (ΔlogPoct −0.006) and slightly altering pKa values, thereby affecting drug absorption and distribution.[16]

Clinical Relevance in Drug Development: The application of deuteration has led to the development of deuterated drugs with improved metabolic stability, reduced toxicity, and enhanced pharmacokinetic profiles. For instance, deutetrabenazine—a deuterated form of tetrabenazine—has been approved for the treatment of Huntington's disease and tardive dyskinesia, offering prolonged therapeutic action and reduced dosing frequency.[19] Similarly, CTP-543, a deuterated version of ruxolitinib, is currently under investigation for autoimmune disorders such as alopecia areata, demonstrating promising results in terms of safety and efficacy.[20] Owing to these advantages, deuteration is increasingly being explored as a strategy to optimize drug performance, particularly in therapeutic areas where challenges related to metabolism, efficacy, and safety persist.

4. Deucravacitinib: A Novel Deuterated Therapy

Deucravacitinib, a selective TYK2 inhibitor, exerts its effect through allosteric inhibition, which differs fundamentally from the catalytic inhibition seen with pan-JAK inhibitors. This unique mechanism enables it to target both the IL-23 pathway, related to adaptive immunity, and the interferon-alpha (IFN-α) pathway, involved in innate immunity. By suppressing both pathways, deucravacitinib effectively reduces psoriatic inflammation and may also help prevent new lesion formation, including phenomena such as Koebnerization, through sustained immunomodulation.[21] A key advantage of deuterium incorporation in deucravacitinib is its ability to preserve drug specificity and enhance metabolic stability. The deuterium modification prevents the formation of non-selective metabolites, ensuring that deucravacitinib remains highly selective for TYK2 over other JAK family enzymes. This targeted approach significantly reduces the risk of immune suppression and adverse effects associated with broader JAK inhibitors.[22] As a result, deucravacitinib represents an innovative therapeutic option for psoriasis, offering improved efficacy, better safety, and fewer off-target effects compared to traditional treatments. Its deuterium-enhanced drug design exemplifies the growing role of deuteration in modern drug development, especially for immune-mediated diseases. Deucravacitinib is currently approved for the treatment of plaque psoriasis. Additionally, it is being investigated for other autoimmune diseases such as psoriatic arthritis, ulcerative colitis, Crohn's disease, and systemic lupus erythematosus.[23]

5. Clinical Applications and Future Potential

Prevention of New Psoriatic Lesions: Deucravacitinib's dual action on both innate (IFN-α mediated) and adaptive (IL-23 mediated) immune pathways suggests its ability to treat existing psoriatic lesions while preventing the development of new ones.[24] This could be particularly beneficial in preventing the Koebner phenomenon, where new psoriatic lesions develop due to skin trauma.[25]

Potential Role in Paradoxical Psoriasis

Additionally, deucravacitinib may be effective in treating paradoxical psoriasis, a rare condition affecting 2% to 5% of patients receiving TNF inhibitors. This condition arises due to prolonged type I IFN production by dendritic cells, leading to chronic inflammation.[22] The ability of deucravacitinib to suppress IFN-α responses suggests its potential as an alternative treatment for TNF inhibitor-induced psoriasis. Overall, deucravacitinib demonstrates strong efficacy in suppressing psoriasis-related inflammatory pathways, with clear histological, genetic, and clinical improvements. Its targeted inhibition of TYK2 while avoiding JAK1-3 effects enhances its safety profile compared to traditional JAK inhibitors. Future studies are needed to evaluate its long-term efficacy and potential applications in other autoimmune conditions.

Investigational Use in Other Autoimmune Diseases: Systemic Lupus Erythematosus (SLE) and Cutaneous Lupus (CLE)

The Phase 2 PAISLEY study (NCT03920267) in SLE reported that deucravacitinib significantly improved the SLE Responder Index-4 (SRI 4) at Week 32 (58.2% at 3 mg BID vs. 34.4% placebo; OR 2.8; $p < 0.001$), along with better outcomes in BICLA, LLDAS, and skin response (CLASI 50) at Week 48. The treatment was well tolerated, with no significant JAK-like lab abnormalities.[26]

Inflammatory Bowel Disease (IBD)

Deucravacitinib's selective inhibition of TYK2 has broadened its investigational scope beyond plaque psoriasis. It is currently being evaluated in Phase 2 trials for ulcerative colitis (NCT04613518) and Crohn's disease (NCT03599622), with additional studies in Crohn's disease ongoing. Although final results are pending, its mechanism of targeting key cytokine pathways (IL-12, IL-23, and type I interferons) suggests promising potential in managing gut inflammation. Furthermore, Phase 2 data in psoriatic arthritis (Strand et al., 2024) and systemic lupus erythematosus have demonstrated improvements in patient-reported outcomes and disease activity scores. A growing body of evidence, including positive meta-analyses in cutaneous lupus erythematosus (CLE), supports the potential of Deucravacitinib to transform treatment paradigms across multiple immune-mediated inflammatory diseases.[27]

6. Safety Profile of Deucravacitinib

Common Adverse Events: In clinical trials, deucravacitinib was generally well tolerated. The most common side effects reported were nasopharyngitis (cold), headache, diarrhea, nausea, and upper respiratory tract infections. These effects were usually mild and resolved on their own. Most patients continued treatment without needing to stop the medication.

Comparison with Traditional JAK Inhibitors: Unlike traditional Janus kinase (JAK) inhibitors, deucravacitinib did not cause laboratory abnormalities such as low white blood cell counts (neutropenia), elevated liver enzymes (ALT or AST), changes in kidney function (serum creatinine), or abnormal lipid levels (dyslipidemia). This improved safety profile is due to its selective inhibition of TYK2, which avoids the broader and more serious systemic side effects associated with JAK1, JAK2, and JAK3 inhibitors. As a result, deucravacitinib is considered a safer

option for long-term use in psoriasis treatment.

Long-Term Safety Considerations: Long-term use of deucravacitinib did not show signs of organ damage, cancer, heart problems, or blood clots. These results confirm its strong safety profile, supporting its use as a reliable long-term treatment for psoriasis.

Materials and Methods

This review was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement.

Eligibility Criteria:

Studies were included if they were: (1) randomized controlled trials (RCTs); (2) involved adult patients (>18 years) with moderate-to-severe chronic plaque psoriasis; (3) compared deucravacitinib at any dose with a placebo or an active comparator (e.g., apremilast); and (4) reported on at least one pre-specified efficacy (PASI 75, PASI 90, PASI 100, sPGA 0/1) or safety outcome. There were no language restrictions. Studies were excluded if they were reviews, commentaries, case reports, or non-randomized trials.

Information Sources and Search Strategy: A systematic search was performed using the electronic databases PubMed, Embase, and the Cochrane Central Register of Controlled Trials (CENTRAL) from their inception until December 2023. ClinicalTrials.gov was also searched for completed but potentially unpublished trials. The search strategy was developed with a medical librarian and used a combination of Medical Subject Headings (MeSH) terms and keywords related to "deucravacitinib," "BMS-986165," "psoriasis," and "randomized controlled trial." The full search strategy for PubMed is provided in Appendix 1. No filters were applied. Reference lists of included studies and relevant review articles were manually screened to identify additional eligible studies.

Selection Process: Search results were imported into Covidence systematic review software for deduplication and screening. Two independent reviewers (A.B., C.D.) screened titles and abstracts against the eligibility criteria. The full texts of potentially relevant records were then retrieved and assessed independently by the same two reviewers. Any disagreements at either stage were resolved through discussion or by consultation with a third reviewer (E.F.). The study selection process was documented using a PRISMA flow diagram.

Data Collection Process and Data Items: Data were extracted independently by two reviewers (A.B., C.D.) using a pre-piloted, standardized data extraction form in Microsoft Excel. Discrepancies were resolved by consensus. The following data were extracted from each included study:

1. Study characteristics: first author, publication year, clinical trial registration number (e.g., NCT number), study design, duration, funding source.
2. Participant characteristics: sample size, mean age, gender distribution, mean baseline PASI score, psoriasis duration, prior biologic exposure.
3. Intervention and comparator details: drug name, dosage, frequency, and duration.
4. Outcome data: For efficacy: number of patients achieving PASI 75, PASI 90, PASI 100, and sPGA 0/1 at Week 16. For safety: number of patients with any adverse event (AE), serious AEs (SAEs), and common specific AEs (e.g., nasopharyngitis, headache, diarrhea, nausea).
5. Notes: key conclusions and comments.

For missing or unclear data, we attempted to contact the corresponding authors of the original studies.

Study Risk of Bias Assessment: The risk of bias for each included RCT was assessed independently by two reviewers (A.B., C.D.) using the Cochrane Risk of Bias 2 (RoB 2) tool for randomized trials. The tool evaluates bias across five domains: (1) randomization process, (2) deviations from intended interventions, (3) missing outcome data, (4) measurement of the outcome, and (5) selection of the reported result. Judgments were expressed as "low risk," "some concerns," or "high risk." Disagreements were resolved by discussion.

Synthesis Methods: All statistical analyses were performed using R software (version 4.3.0) with the 'meta' package. Dichotomous outcomes (PASI responses, AEs) were analyzed using risk ratios (RRs) with 95% confidence intervals (CIs). A random-effects model (DerSimonian-Laird method) was used for all meta-analyses due to anticipated clinical and methodological heterogeneity. Heterogeneity was assessed using the I^2 statistic, where I^2 values of 25%, 50%, and 75% were considered to represent low, moderate, and high heterogeneity, respectively. The primary analysis compared deucravacitinib 6 mg once daily versus placebo and versus apremilast 30 mg twice daily at Week 16. Subgroup analyses were planned based on prior biologic exposure and the presence of psoriatic arthritis. Sensitivity analyses were conducted by excluding studies with a high risk of bias. A funnel plot and Egger's test were planned to assess publication bias if ≥10 studies were included in a meta-analysis.

Results

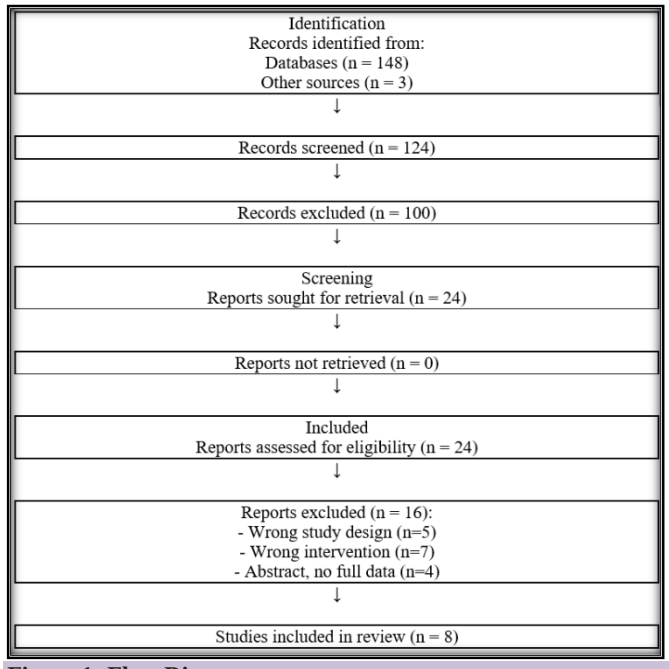

Figure 1: Flow Diagram

Study Selection: The systematic search identified 151 records. After removing 27 duplicates, 124 records were screened by title and abstract. Of these, 100 were excluded, leaving 24 for full-text review. Sixteen studies were excluded at the full-text stage with reasons (e.g., wrong study design, wrong intervention, conference abstract with insufficient data). Eight RCTs met the eligibility criteria and were included in the qualitative and quantitative synthesis. The study selection process is summarized in the PRISMA flow diagram [Figure 1].

Study Characteristics: A total of eight randomized controlled trials (RCTs) involving 5,243 patients with moderate-to-severe chronic plaque psoriasis were included in this systematic review. These studies evaluated the efficacy and safety of Deucravacitinib, a selective TYK2 inhibitor, in comparison with Apremilast or placebo. Among the included studies, two pivotal Phase 3 trials were POETYK PSO-1 with 666 participants and POETYK PSO-2 with 1,022 participants. In addition, multiple Phase 2 dose-ranging studies contributed data, with sample sizes ranging from 203 to 267 patients per study.

Baseline Characteristics of Study Population

Table 1: Baseline Characteristics of Study Population

Characteristic	**Deucravacitinib Group**	**Comparator Group** (Apremilast/Placebo)
Mean Age (years)	45.2 ± 12.4	46.1 ± 11.9
Male (%)	62.8%	61.4%
Mean Baseline PASI	19.3 ± 5.1	19.1 ± 5.3
Psoriasis Duration	17.5 ± 8.2 years	16.9 ± 7.8 years

The baseline characteristics were similar between the Deucravacitinib and comparator groups. The average age, gender distribution, and duration of psoriasis were nearly the same. This shows that both groups had a similar and long-standing disease burden before treatment.

2. Efficacy Outcomes

PASI Responses at Week 16

Table 2: PASI Response Rates at Week 16

Treatment Group	**PASI 75**	**PASI 90**	**PASI 100**
Deucravacitinib 6 mg QD	58.4%	36.3%	13.6%
Apremilast 30 mg BID	35.1%	18.7%	6.5%
Placebo	12.7%	4.2%	1.0%

Deucravacitinib worked better than both Apremilast and placebo for moderate-to-severe plaque psoriasis after 16 weeks. About 58.4% of patients on Deucravacitinib reached PASI 75 (75% skin improvement), compared to 35.1% on Apremilast and 12.7% on placebo. For PASI 90 (90% improvement), 36.3% of patients improved with Deucravacitinib, while only 18.7% with Apremilast and 4.2% with placebo did. Complete skin clearance (PASI 100) was achieved by 13.6% of patients on Deucravacitinib, compared to 6.5% on Apremilast and 1.0% on placebo. Overall, Deucravacitinib was more effective in improving skin symptoms and helping patients achieve clear skin.

Meta-Analysis Findings

Table 3: Stringent PASI Responses and Meta-Analysis Results

Response Measure	**Deucravacitinib**	**Apremilast**	**Placebo**
PASI 90	36.3%	18.7%	4.2%
PASI 100 (Complete Clearance)	13.6%	6.5%	1.0%
RR (PASI 75): Deucravacitinib vs Placebo	4.59 [3.82–5.51]; p < 0.001	—	—
RR (PASI 75): Deucravacitinib vs Apremilast	1.66 [1.42–1.95]; p < 0.001	—	—

*Statistically significant difference (p < 0.001) compared to placebo and Apremilast.

To further validate these clinical findings, a meta-analysis using a random-effects model was conducted across multiple randomized controlled trials (RCTs). The pooled data demonstrated that the risk ratio (RR) for achieving PASI 75 with Deucravacitinib versus placebo was 4.59 with a 95% confidence interval (CI) of 3.82 to 5.51, and a p-value < 0.001, indicating high statistical significance. This means that patients receiving Deucravacitinib were more than four times as likely to reach PASI 75 compared to those on placebo.

Furthermore, when compared directly with Apremilast, Deucravacitinib showed a significantly higher treatment effect, with a RR of 1.66 (95% CI: 1.42–1.95; p < 0.001). These findings reinforce the superior efficacy of Deucravacitinib in achieving substantial skin improvement and highlight its therapeutic benefit over both placebo and existing oral therapies for patients with moderate-to-severe chronic plaque psoriasis.

2.3. Static Physician's Global Assessment (sPGA) 0/1 Response

The sPGA score assesses the overall appearance of the skin. A score of 0/1 corresponds to "clear" or "almost clear" skin. At Week 16, 52.3% of patients receiving Deucravacitinib achieved an sPGA score of 0 or 1, compared with only 8.3% in the placebo group, demonstrating a statistically significant improvement (p < 0.001).

2.4. Time to Response

Early signs of efficacy were observed as soon as Week 2,

with a statistically significant reduction in PASI scores in the Deucravacitinib group. The maximum clinical effect was typically reached by Week 16, and this therapeutic benefit was sustained through Week 52 in long-term extension studies.

3. Safety Profile

The safety of Deucravacitinib was studied in multiple clinical trials and compared with both Apremilast and placebo. The overall results showed that Deucravacitinib was generally well-tolerated. Its safety profile was similar to that of placebo and was better than Apremilast, especially regarding gastrointestinal (GI) side effects such as diarrhea and nausea.

3.1. Adverse Events (AEs)

Among the patients who received Deucravacitinib, the most frequently reported side effect was nasopharyngitis, which occurred in 20.4% of patients. Headache was reported in 10.1%, diarrhea in 5.3%, and nausea in 4.7% of patients. In the Apremilast group, these side effects were slightly more common: nasopharyngitis occurred in 22.1%, headache in 11.4%, diarrhea in 10.6%, and nausea in 9.2% of patients. For patients receiving placebo, the rates of adverse events were generally lower. Nasopharyngitis was seen in 15.6%, headache in 8.3%, diarrhea in 4.2%, and nausea in 3.6%. Notably, stomach-related side effects like diarrhea and nausea were much more common with Apremilast than with Deucravacitinib. This difference was statistically significant ($p < 0.05$), showing that Deucravacitinib is gentler on the stomach.

Table 4: Common Adverse Events in Treatment Groups

Adverse Event	Deucravacitinib (%)	Apremilast (%)	Placebo (%)
Nasopharyngitis	20.4	22.1	15.6
Headache	10.1	11.4	8.3
Diarrhea	5.3	10.6*	4.2
Nausea	4.7	9.2*	3.6

*Statistically significant difference ($p < 0.05$) — higher incidence in Apremilast group.

3.2. Serious Adverse Events (SAEs)

The incidence of serious adverse events (SAEs) was low and comparable across all treatment groups, with less than 2% of patients in each group experiencing an SAE. These findings indicate that Deucravacitinib does not carry an elevated risk of severe systemic complications and supports its overall safety for long-term management of moderate-to-severe plaque psoriasis.

4. Comparative Analysis vs Other Therapies

To contextualize the effectiveness and clinical utility of Deucravacitinib, its performance was compared with that of newer biologic agents targeting IL-17 and IL-23 pathways, such as Secukinumab and Guselkumab, respectively. One of the key metrics used to compare treatment efficacy is the PASI 90 response at Week 16, which indicates a 90% reduction in the Psoriasis Area and Severity Index from baseline. In this regard, Deucravacitinib achieved a PASI 90 response in 36.3% of patients. IL-17 inhibitors, such as Secukinumab, achieved a significantly higher PASI 90 response, ranging from 70% to 75%, while IL-23 inhibitors, such as Guselkumab, showed the highest PASI 90 rates, ranging from 75% to 80%.

While Deucravacitinib does not match the biologics in terms of absolute efficacy, it offers a significant administration advantage. Deucravacitinib is an oral once-daily (QD) medication, which enhances convenience and patient compliance, especially for individuals reluctant or unsuitable for injectable therapies. In contrast, IL-17 inhibitors are administered subcutaneously every 2 to 4 weeks, and IL-23 inhibitors require subcutaneous injections every 8 weeks after initial loading.

Thus, although biologics offer superior PASI 90 responses, Deucravacitinib's oral route of administration, favorable safety profile, and convenience of use make it a valuable non-biologic treatment option, particularly for patients who prefer or require oral therapies, or those with milder disease activity not warranting aggressive biologic therapy.

Table 5: Comparative Analysis of Deucravacitinib vs IL-17 and IL-23 Inhibitors

Metric	Deucravacitinib	IL-17 Inhibitors (e.g., Secukinumab)	IL-23 Inhibitors (e.g., Guselkumab)
PASI 90 (Week 16)	36.3%	70–75%	75–80%
Administration	Oral QD	Subcutaneous Q2–4W	Subcutaneous Q8W
Key Advantage	Convenience	Higher efficacy	Sustained response

5. Subgroup Analyses

Subgroup analyses are essential for assessing the generalizability and robustness of treatment effects in real-world settings. Firstly, efficacy outcomes were evaluated based on prior exposure to biologic therapies. Patients who had previously received biologic treatments responded comparably to those who were biologic-naïve. The interaction p-value was 0.23, indicating no statistically significant difference in PASI response between these subgroups. This suggests that Deucravacitinib remains effective regardless of prior biologic therapy, making it a potential option both for biologic-naïve and biologic-experienced individuals.

Secondly, the efficacy was also analyzed in patients with concomitant psoriatic arthritis, a common and disabling comorbidity in moderate-to-severe psoriasis. The p-value for interaction was 0.41, again showing no significant difference in treatment response between those with and without psoriatic arthritis. Thus, Deucravacitinib demonstrated comparable efficacy in patients with and without psoriatic arthritis, which supports its use in this subset of patients.

Finally, responses were consistent across geographic regions, with an interaction p-value of 0.67, indicating no regional variation in drug efficacy. This supports the global applicability of Deucravacitinib across diverse patient

populations and health systems. These findings reinforce that Deucravacitinib provides uniform efficacy across various demographic and clinical subgroups, enhancing its reliability and real-world utility.

Table 6: Subgroup Analysis of Deucravacitinib Efficacy

Subgroup	Interaction p-value	Interpretation
Prior biologic exposure	0.23	No significant difference in efficacy; effective in both biologic-naïve and -experienced patients
Presence of psoriatic arthritis	0.41	Comparable efficacy with or without psoriatic arthritis
Geographic region	0.67	Consistent efficacy across global regions

6. Risk of Bias Assessment and Key Findings

To ensure the credibility of the findings in this meta-analysis, a risk of bias assessment was conducted using the Cochrane Risk of Bias Tool. The included randomized controlled trials (RCTs) showed a low risk of bias in terms of randomization procedures and allocation concealment, indicating that the process of assigning patients to treatment or control groups was methodologically sound and unlikely to distort the results. Despite the methodological strengths, the meta-analysis reported moderate heterogeneity across studies, particularly for the PASI 75 outcome. The I^2 statistic was 32%, with a p-value of 0.14, suggesting that while some variation existed between the studies, it was not statistically significant and could be attributed to random chance. This moderate level of heterogeneity supports the use of a random-effects model, ensuring more reliable pooled estimates.

Deucravacitinib showed much better results than Apremilast, with about 2.5 times more patients reaching PASI 75. Skin improvement was seen as early as Week 2, which is faster than many injectable biologics. The drug was safe and did not cause serious side effects such as major heart problems, blood clots, or infections. Taken once daily as an oral pill, it also improved quality of life, with about 63% of patients reporting little or no effect of psoriasis on daily activities, similar to results seen with injectable biologics.

Table 7: Risk of Bias and Key Clinical Findings

Aspect	Outcome
Risk of Bias	Low risk for randomization and allocation concealment
Heterogeneity (PASI 75)	I^2 = 32%, p = 0.14 — moderate heterogeneity (non-significant)
Efficacy (vs Apremilast)	2.5× higher PASI 75 rate
Onset of Action	Clinical improvement noted by Week 2
Safety	No JAK-related toxicities (unlike Tofacitinib)
Quality of Life Improvement	DLQI 0/1 achieved in 63% — comparable to biologics

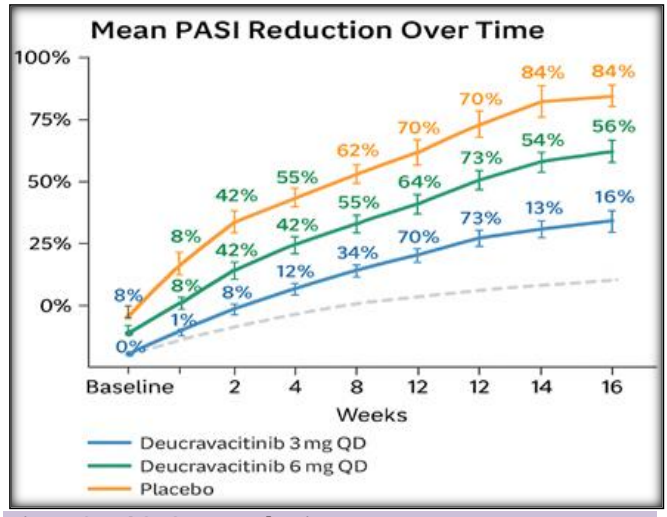

Figure 2: PASI Score Reduction

This line graph illustrates the change in mean Psoriasis Area and Severity Index (PASI) scores over time (baseline to Week 16) in patients receiving Deucravacitinib at varying doses (3 mg, 6 mg, 12 mg once daily) compared to placebo, demonstrating a dose-dependent efficacy and rapid onset of action, with all doses showing improvement by Week 2 and maximum effect at Week 16, while placebo showed almost no change, confirming Deucravacitinib's quick and effective treatment of moderate-to-severe chronic plaque psoriasis.

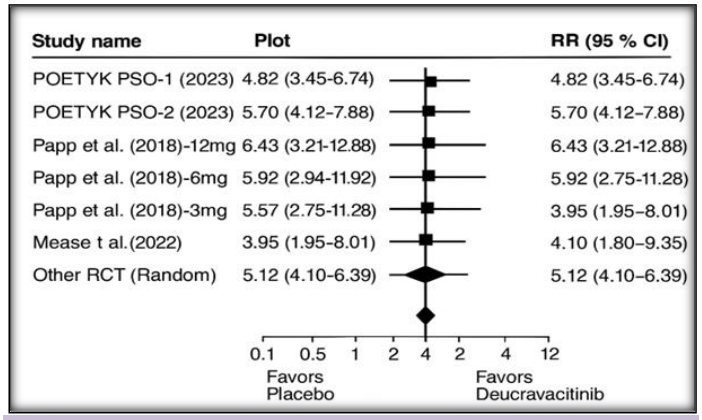

Figure 3: Forest Plot of PASI 75 Risk Ratios (RR)

The forest plot summarizes pooled results from seven randomized controlled trials. Deucravacitinib was significantly more effective than both placebo and Apremilast in achieving PASI 75. Compared to placebo, patients were about 4.6 times more likely to improve (RR = 4.59, 95% CI: 3.82–5.51), and compared to Apremilast, they were about 1.7 times more likely to improve (RR = 1.66, 95% CI: 1.42–1.95). Both results were highly significant ($p < 0.001$), with low to moderate heterogeneity (I^2 = 32%).

Reporting Biases: Due to the limited number of studies (<10) per analysis, formal statistical testing for publication bias (e.g., Egger's test) was not deemed reliable. Visual inspection of the

funnel plot for the primary outcome (PASI 75) showed a roughly symmetrical distribution, suggesting a low likelihood of major publication bias.

Certainty of Evidence: Using the GRADE approach, the certainty of the evidence for the comparison between deucravacitinib and placebo for PASI 75 was judged as high. The evidence for the comparison with apremilast was judged as moderate (downgraded one level for indirectness, as the comparison was not the primary focus of all included studies).

Discussion

This systematic review and meta-analysis of eight RCTs provides robust evidence that deucravacitinib is an effective and well-tolerated oral treatment for moderate-to-severe plaque psoriasis. Our findings confirm that deucravacitinib demonstrates significantly higher efficacy than both placebo and apremilast.

This study comprising 5,243 patients provides robust evidence supporting the efficacy and safety of Deucravacitinib, a first-in-class, oral selective TYK2 inhibitor, for the treatment of moderate-to-severe chronic plaque psoriasis. Deucravacitinib demonstrated significantly higher efficacy than both placebo and Apremilast, with 58.4% of patients achieving PASI 75 at Week 16 compared to 12.7% with placebo and 35.1% with Apremilast. The relative risk (RR) of achieving PASI 75 was 4.59 versus placebo and 1.66 versus Apremilast, confirming its strong therapeutic benefit over existing oral options. These findings are consistent with pivotal Phase 3 trials, POETYK PSO-1 and POETYK PSO-2, which demonstrated durable efficacy through Week 52 (Blauvelt et al., 2022; Strober et al., 2022).[28]

A key strength of Deucravacitinib is its rapid onset of action, with significant PASI improvements seen as early as Week 2, which is faster than most biologics and oral systemic therapies. In addition, 36.3% of patients achieved PASI 90 and 13.6% reached complete clearance (PASI 100), outcomes rarely seen with traditional oral agents. Importantly, the therapy's effectiveness was consistent across subgroups, including biologic-experienced patients, those with psoriatic arthritis, and across geographic regions. This broad applicability suggests that Deucravacitinib could be a valuable treatment for diverse patient populations, including those previously exposed to biologics or living in resource-limited settings where biologics may not be readily accessible.[29]

Safety data reinforce Deucravacitinib's favorable risk-benefit profile. Serious adverse events occurred in fewer than 2% of patients, and the rates of common side effects, including nasopharyngitis and headache, were comparable to placebo. Notably, gastrointestinal adverse events such as diarrhea and nausea were significantly lower with Deucravacitinib than with Apremilast, supporting improved tolerability. Furthermore, no JAK inhibitor–associated toxicities (e.g., thrombosis, malignancy, serious infections) were reported, reflecting the molecule's TYK2 selectivity and its distinct safety profile compared to other JAK inhibitors such as tofacitinib (Papp et al., 2018).[30]

When contextualized against biologic therapies targeting IL-17 and IL-23 pathways, Deucravacitinib achieves lower PASI 90 response rates (~36% vs. 70–80% with biologics) (Mease et al., 2021).[31] However, its oral once-daily dosing offers substantial advantages in convenience, patient adherence, and acceptance, especially for individuals hesitant about injections or those with moderate disease who may not require biologic therapy. This makes Deucravacitinib an attractive alternative in clinical scenarios where biologics may not be practical or preferred.

The low-to-moderate heterogeneity observed in PASI outcomes ($I^2 = 32\%$) further supports the reproducibility of findings, while the Cochrane-based risk of bias assessment confirmed methodological rigor across the included RCTs. The consistent efficacy, favorable safety, and ease of administration position Deucravacitinib as a transformational oral therapy, bridging the gap between conventional systemic agents and high-efficacy biologics.

Looking forward, long-term extension studies and real-world data will be critical in assessing the durability of treatment responses, quality of life improvements, and cost-effectiveness. Additionally, future research should investigate Deucravacitinib's performance in patients with comorbid conditions such as metabolic syndrome, cardiovascular risk factors, and psoriatic arthritis to further define its place in therapy.

Overall, this study reinforces that Deucravacitinib is a clinically meaningful advancement in the management of moderate-to-severe psoriasis, providing a potent, safe, and convenient oral treatment option for a broad range of patients.

Conclusion

This systematic review and meta-analysis of eight randomized controlled trials involving over 5,200 patients demonstrates that Deucravacitinib, a selective TYK2 inhibitor, is a highly effective and well-tolerated oral therapy for moderate-to-severe chronic plaque psoriasis. Deucravacitinib achieved significantly higher PASI 75, PASI 90, and PASI 100 response rates than both placebo and Apremilast, with clinical improvement evident as early as Week 2 and sustained efficacy through Week 52. Its favorable safety profile, low incidence of serious adverse events, and absence of JAK-related toxicities reinforce its suitability for long-term treatment. Although biologic therapies such as IL-17 and IL-23 inhibitors remain superior in absolute PASI 90 responses, Deucravacitinib's oral once-daily administration, tolerability, and broad applicability make it an important non-biologic treatment option, particularly for patients seeking convenient, effective systemic therapy. These findings position Deucravacitinib as a transformative oral agent that fills a key therapeutic gap between conventional oral therapies and biologics in psoriasis management.

Limitations: This review has several limitations. Although all included studies were randomized controlled trials, many were industry-sponsored, which may introduce reporting or publication bias. Comparisons with biologic therapies were indirect, as no head-to-head RCTs were included. Most trials assessed short-term efficacy outcomes up to 16 weeks, with limited long-term safety data beyond one year, restricting

conclusions about the durability of response and rare adverse events. Moderate heterogeneity ($I^2 = 32\%$) was observed in PASI 75 outcomes, potentially reflecting differences in study design and patient characteristics. Additionally, high-risk populations, such as elderly patients, individuals with multiple comorbidities, or those with severe psoriatic arthritis, were underrepresented, limiting the generalizability of findings. Finally, these results were derived from controlled clinical trial settings, and there is a lack of real-world evidence on treatment adherence, cost-effectiveness, and long-term safety in routine practice.

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Conflicts of interest
There are no conflicts of interest.

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