Therapeutics and Clinical Risk Management

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REVIEW

Clinical Utility of Deucravacitinib for the Management of Moderate to Severe Plaque Psoriasis

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Introduction: Psoriasis is a chronic, immune-mediated skin condition with significant detriments to physical/mental health. While systemic therapies are available for the treatment of moderate-to-severe psoriasis, patients can experience therapeutic failure, loss of efficacy, or medical contraindications that require other therapeutic options.

Objective: With the recent approval of deucravacitinib, a first-in-class TYK2 small molecule inhibitor administered orally for psoriasis patients, we reviewed data from randomized controlled trials (RCTs) to synthesize its clinical utility. To our knowledge, this is the first systematic review and meta-analysis of deucravacitinib comparing its clinical efficacy to placebo in psoriasis.

Methods: A literature search was conducted in PubMed (MEDLINE), Embase, and the Cochrane Central Register of Controlled Trials to identify RCTs studying deucravacitinib in human patients with moderate-to-severe psoriasis.

Results: One placebo-controlled Phase II RCT and two placebo-controlled/active-comparator Phase III RCTs were included for review. Patients (N=1953) treated with deucravacitinib 6 mg daily showed marked improvement in disease severity (Psoriasis Area and Severity Index (PASI), static Physician Global Assessment (sPGA) and quality-of-life outcomes compared to patients administered comparator (apremilast) and placebo. Clinical improvement given deucravacitinib was noted for scalp psoriasis but not fingernail psoriasis. Meta-analysis (deucravacitinib, n=888; placebo, n=466) comparing rates of clearance (sPGA 0/1) demonstrated superior efficacy of deucravacitinib compared to placebo (odds ratio, 12.87; 95% confidence interval, 8.97–18.48; χ^2=4.08, I^2=51%). Deucravacitinib was well-tolerated, with similar rate of occurrence and type of adverse events reported among patients treated with placebo or apremilast at Week 12–16. No cardiovascular events, serious infections, or lab abnormalities were noted.

Conclusion: Deucravacitinib possesses good efficacy, with no report of safety concerns associated with prior JAK inhibitors used for psoriasis. Meta-analysis demonstrated deucravacitinib's superiority compared to placebo, indicating its promising clinical utility. Further studies are needed to observe long-term safety and efficacy, and to compare deucravacitinib to existing treatments.

Keywords: apremilast, deucravacitinib, meta-analysis, placebo, plaque psoriasis, systematic review

Introduction

Psoriasis is a chronic inflammatory disorder of the skin and joints that affects 8 million Americans and 2–3% of the population globally.[1] Psoriasis has a profound impact on both the physical and psychosocial health of those affected. Patients are subject to increased risk of developing comorbid systemic disease, including cardiovascular disease, diabetes, anxiety, depression, and all-cause mortality.[2]

A variety of therapies are available for the treatment of psoriasis, including topical medications, phototherapy, oral and biologic agents. Oral immunosuppressants such as methotrexate and cyclosporine may be highly effective for some patients, but such treatments have significant potential for adverse effects.[3] For individuals with a more severe psoriatic disease course, treatment with a systemic therapy such as a biologic agent is often required. Recent advancements surrounding new targeted agents have yielded promising results; here, we review the clinical potential of deucravacitinib

Received: 29 March 2023
Accepted: 15 May 2023
Published: 18 May 2023

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(ie, BMS-986165, Sotyktu™), a new oral small molecule approved by the US Food and Drug Administration (FDA) in September 2022 for the treatment of moderate-to-severe psoriasis.

TYK2 Signaling and Psoriasis Pathogenesis

The pathogenesis of psoriasis is characterized by aberrant keratinocyte differentiation and excessive growth of the epidermis, leading to the formation of erythematous patches and plaques with thick overlying scale.[4] Psoriasis pathogenesis involves a complex interplay of genetic (eg, susceptibility alleles) and environmental factors, which can combine to trigger systemic inflammatory cascades leading to disease presentation.[4] While psoriatic immune dysregulation is complex and not fully elucidated, T helper 17 (Th17) cells are known to be a central component that, when aberrantly activated, produce important effector cytokines acting in a positive feedback loop to recruit additional immune cells and accelerate psoriasis development.[5,6]

Involvement of the interleukin (IL)-23/IL17 pathway mediates psoriasis via the activation and promotion of keratinocyte proliferation.[5] Cytokines like TNF-α, IL-17, and IL-23 are the targets of biologic agents used in psoriasis.[7,8] Many of these same cytokines, including IL-23, bind to type I and II cytokine receptors, which possess no inherent catalytic activity and must rely on Janus kinase (JAK) proteins to mediate their effects.[7] Tyrosine kinase 2 (TYK2) is one of four members of the JAK family of proteins.[7]

JAK/STAT signaling refers to a system comprised of a dimeric transmembrane cytokine receptor, a pair of intracellular JAKs, and a family of Signal Transducers and Activators of Transcription (STATs).[7] Upon binding of a cytokine to its receptor, a conformational change in the receptor proteins occur, leading to autophosphorylation of intracellular JAKs.[7] This enables another conformational change leading to the phosphorylation of STATs, which then dissociate from the receptor complex before translocating to the nucleus and acting as transcription factors.[7]

TYK2 pairs with other JAK family members to mediate the signaling of IL-12 and IL-23 receptors, as well as type I IFN receptors; TYK2 inhibition leads to reduced Th17 cell polarization, increased suppressive functions of regulatory T cells, and additional downstream effects protective against psoriasis development.[9–12] Given TYK2's role downstream of current biologic targets such as IL-12 and IL-23, TYK2 inhibition may serve as a promising strategy that can address existing challenges in the treatment of moderate-to-severe psoriasis.[12]

Deucravacitinib

In September 2022, deucravacitinib—an oral, first-in-class, small molecule, selective allosteric inhibitor of TYK2—was approved by the FDA for the treatment of psoriasis in the U.S.[13] Deucravacitinib binds to the catalytically inactive pseudokinase regulatory domain of TYK2 and stabilizes an inhibitory interaction between the regulatory and catalytic domains.[13] Through this method, TYK2 is inactivated and cannot interact with other receptors to lead to downstream signal transduction.[11,14] In preclinical studies, deucravacitinib was revealed to inhibit TYK2 with high selectivity and minimal off-target effects on other JAK family members,[11,14] suggesting that deucravacitinib may possess an improved safety profile compared to less specific JAK inhibitors, which have been associated with hyperlipidemia, increased risk of infections, and other systemic changes.[14–16]

Given recent FDA-approval and promising clinical data, we aimed to investigate deucravacitinib's clinical utility for the treatment of moderate-to-severe psoriasis. To our knowledge, no systematic review has been conducted—here, we performed a systematic review with meta-analysis to synthesize the findings from randomized controlled trials (RCTs) studying deucravacitinib for psoriasis.

Materials and Methods

As a review, all data used were non-identifiable and publicly available; institutional review board approval was not required at the University of California, San Francisco. The study protocol and design are reported according to the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols 2020 guidelines.[17] A literature search was conducted in PubMed (MEDLINE), Embase, and the Cochrane Central Register of Controlled Trials (CENTRAL) in March 2023 using a combination of the terms ("deucravacitinib" OR "sotyktu") AND ("psoriasis").

Study Design and Eligibility Criteria

The efficacy of new psoriasis treatments is measured in clinical trials via standardized, objective disease severity metrics, including the Psoriasis Area and Severity Index (PASI) and Physician Global Assessment (PGA).[18,19] These tools utilize grading scales to stratify disease severity based on clinical characteristics including body surface area involvement and degree of erythema, induration, and scaling. Given the impact psoriatic disease has on patients' psychosocial health and quality of life, concomitant assessment of these domains with tools such as the Dermatology Life Quality Index (DLQI) is appropriate and often co-reported in clinical trials or post hoc studies.[19]

Studies included in this review were RCTs investigating human subjects with moderate-to-severe psoriasis (thus, only Phase II trials and above, as Phase I trials were conducted in healthy participants),[20] defined in clinical trials as static PGA (sPGA) ≥3, PASI ≥12, and body surface area (BSA) ≥10%, treated with deucravacitinib. RCTs that studied psoriatic arthritis but not psoriasis were excluded.[21] Study characteristics including clinical trial name/number, number of patients, intervention dose and frequency, treatment duration, clinical efficacy, and safety outcomes were obtained using a standardized table tailored to this review.

Study Selection and Data Extraction

Initial screening of studies was performed manually by two independent reviewers (J.Q.J., R.K.S.). Any queries in eligibility criteria were resolved via adjudication by an additional reviewer (W.L.). Data abstraction was performed by two independent reviewers (J.Q.J., R.K.S.). All randomized studies included for analysis were assessed for risk of bias by two independent authors (J.Q.J., R.K.S.) using the Critical Appraisal Skills Programme (CASP) checklist for RCTs.[22]

Primary outcomes sought for the purpose of this review included an sPGA of 0 or 1 (indicating clear or almost clear disease). Secondary outcomes included an sPGA of 0, a 75%, 90%, or 100% improvement in the PASI score (ie, PASI 75, PASI 90, or PASI 100), a DLQI score of 0 or 1, scalp-specific PGA (ss-PGA) of 0 or 1, and a PGA of Fingernail Psoriasis (PGA-F) of 0 or 1. The final endpoint was determined to be Week 12–16, as all included studies reported efficacy measures within this timepoint.

Statistical Analysis

Meta-analysis was performed using the Cochrane Review Manager 5.4 application comparing the sPGA 0/1 rates of deucravacitinib versus placebo. Only data from patients receiving the FDA-approved dose of deucravacitinib (6 mg per day) or placebo were included for meta-analysis. An odds ratio (OR) was calculated using the Mantel-Haenszel fixed-effects method, which was chosen over the Peto method as the latter is better suited for rare event occurrences.[23] Significance of heterogeneity was assessed using the χ^2 test ($P < 0.1$ set as statistically significant) and presented as the I^2 test ($I^2 > 50\%$ indicates significant heterogeneity, $I^2 < 25\%$ indicates non-significant heterogeneity).

Results

Following the application of inclusion and exclusion criteria (PRISMA diagram shown in Figure 1), three RCTs were included for review, including one Phase II placebo-controlled trial (NCT02931838)[24] and two Phase III placebo-controlled and active-comparator (apremilast) RCTs (POETYK PSO-1, POETYK PSO-2).[25,26] The three RCTs were composed of a total of 1953 patients with moderate-to-severe psoriasis—including 1065 treated with deucravacitinib, 422 treated with apremilast, and 466 who received placebo. Overall, deucravacitinib patients showed marked improvement in disease severity and quality-of-life outcomes compared to apremilast and placebo groups; deucravacitinib patients with scalp psoriasis demonstrated marked improvement compared to apremilast and placebo groups, but improvements in fingernail psoriasis measures were not significant (Table 1). The risk of bias assessment of all studies is presented in Table 2.

Clinical Outcomes of Included Studies

NCT02931838 was a 12-week, randomized, placebo-controlled, dose-ranging Phase II clinical trial that included 267 adults with moderate-to-severe plaque psoriasis (sPGA ≥3, PASI ≥12, and BSA ≥10%; mean baseline PASI was 18).[24] The primary clinical outcome assessed was PASI 75 at Week 12 compared to baseline. Patients were randomly assigned

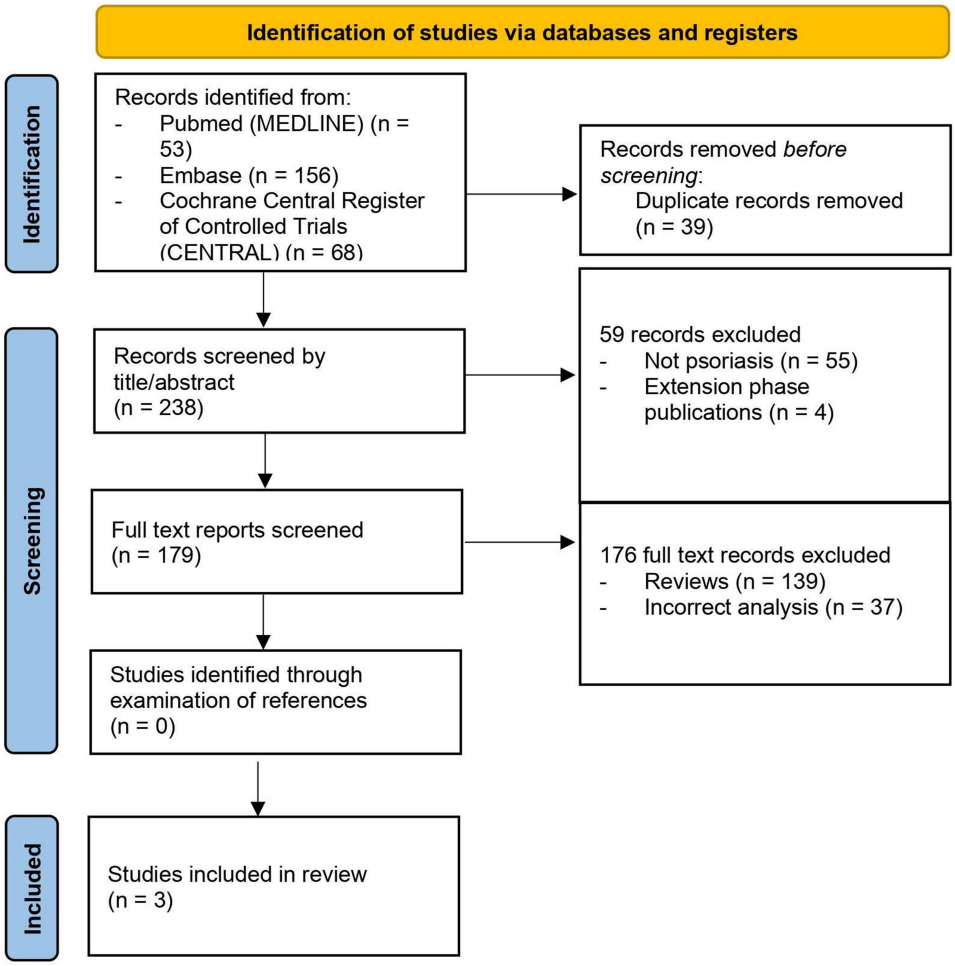

Figure 1 PRISMA diagram showing study selection.

to one of six groups to receive placebo medication or deucravacitinib orally at the following frequencies: 3 mg every other day (QOD), 3 mg daily (QD), 3 mg twice daily (BID), 6 mg BID, or 12 mg QD. Detailed clinical outcomes can be found in Table 1; improvements in PASI scores were associated with higher doses of deucravacitinib and were improved compared to placebo groups. Nearly 70% of the cohort that received deucravacitinib 3 mg BID (closest to the FDA-approved dosage of 6 mg once daily) achieved PASI 75 at Week 12, compared to 6.7% of the placebo cohort. Improvements in clinical outcomes were correlated with biomarker changes and patient-reported quality-of-life (percent of patients who achieved DLQI 0/1).[27]

POETYK PSO-1 (NCT03624127) and POETYK PSO-2 (NCT03611751) were randomized, double-blind, double-dummy Phase III trials that compared the efficacy and safety of deucravacitinib versus an active-comparator (apremilast) and placebo.[25,26] A total of 666 patients (PSO-1) and 1020 patients (PSO-2) were randomized 2:1:1 to deucravacitinib 6 mg QD, apremilast 30 mg BID, or placebo. All participants receiving placebo were crossed over to receive deucravacitinib at Week 16; patients receiving apremilast who did not achieve PASI 50 (PSO-1) or PASI 75 (PSO-2) by Week 16 were also switched to the deucravacitinib group. In PSO-2, deucravacitinib patients achieving PASI 75 at Week 24 were re-randomized 1:1 to deucravacitinib at the same dosing schedule or placebo for the remainder of the study. If the newly switched placebo patients exhibited disease relapse, they were re-started on deucravacitinib.

Detailed clinical outcomes for both studies are reported in Table 1; briefly, deucravacitinib was shown to be more effective than both comparator and placebo at Week 16 for both primary endpoints assessed (PASI 75 and sPGA 0/1). The percent of patients who achieved PASI 75 in PSO-1 and PSO-2 (vs apremilast, placebo) were 58.7% (vs 35.1%,

Table 1 Clinical Outcomes Reported in Deucravacitinib Randomized Controlled Trials for Moderate-to-Severe Psoriasis

Study		Percentage (%) of Patients Who Achieved…							
		PASI 75	**PASI 90**	**PASI 100**	**sPGA 0/1**	**sPGA 0**	**ss-PGA 0/1**	**DLQI 0/1**	**PGA-F 0/1**
NCT02931838[24]	Week 12	DEU 3 mg QOD 9.1 DEU 3 mg QD 38.6 DEU 3 mg BID 68.9 DEU 6 mg BID 66.7 DEU 12 mg QD 75.0 PBO 6.7 [*P* = 0.4873, 0.0003, <0.0001]	DEU 3 mg QOD 6.8 DEU 3 mg QD 15.9 DEU 3 mg BID 44.4 DEU 6 mg BID 44.4 DEU 12 mg QD 43.2 PBO 2.2 [*P* = 0.4873, 0.0003, <0.0001]	DEU 3mg QOD 2.3 DEU 3 mg QD 0 DEU 3 mg BID 8.9 DEU 6 mg BID 17.8 DEU 12 mg QD 25.0 PBO 0	DEU 3mg QOD 20.5 DEU 3 mg QD 38.6 DEU 3 mg BID 75.6 DEU 6 mg BID 64.4 DEU 12 mg QD 75.0 PBO 6.7	N/A	N/A	DEU 3mg QOD 4.4 DEU 3 mg QD 15.9 DEU 3 mg BID 15.9 DEU 6 mg BID 42.2 DEU 12 mg QD 60.0 PBO 63.6	N/A
POETYK PSO-1[25]	Week 16	DEU 58.7 APR 35.1 PBO 12.7 [*P* < 0.0001]	DEU 35.5 APR 19.6 PBO 4.2 [*P* = 0.0002, <0.0001]	DEU 14.2 APR 3.0 PBO 0.6 [*P* < 0.0001]	DEU 53.6 APR 32.1 PBO 7.2 [*P* < 0.0001]	DEU 17.5 APR 4.8 PBO 0.6 [*P* < 0.0001]	DEU 70.3 APR 39.1 PBO 17.4 [*P* < 0.0001]	DEU 7.9 APR 4.4 PBO 0.7 [*P* = 0.0088, <0.0001]	DEU 20.9 PBO 8.8 (n = 43, 34)
	Week 24	DEU 69.3 APR 38.1 [*P* < 0.0001]	DEU 42.2 APR 22.0 [*P* < 0.0001]	DEU 17.5 APR 6.5 [*P* = 0.0007]	DEU 58.7 APR 31.0 [*P* < 0.0001]	DEU 18.1 APR 6.5 [*P* = 0.0004]	DEU 72.2 APR 42.7 [*P* < 0.0001]	DEU 48.1 APR 24.2 [*P* < 0.0001]	N/A
POETYK PSO-2[26]	Week 16	DEU 53.0 APR 39.8 PBO 9.3 [*P* = 0.0004, <0.0001]	DEU 27.0 APR 18.1 PBO 2.7 [*P* = 0.0046, <0.0001]	DEU 10.2 APR 4.3 PBO 1.2 [*P* = 0.0051, <0.0001]	DEU 49.5 APR 33.9 PBO 8.6 [*P* < 0.0001]	DEU 15.7 APR 6.3 PBO 1.2 [*P* = 0.0002, <0.0001]	DEU 59.7 APR 36.7 PBO 17.3 [*P* < 0.0001]	DEU 37.6 APR 23.1 PBO 9.8 [*P* < 0.0001]	DEU 20.3 PBO 7.9 [*P* = 0.062] (n = 69, 38)
	Week 24	DEU 58.7 APR 37.8 [*P* < 0.0001]	DEU 32.5 APR 19.7 [*P* < 0.0001]	DEU 13.1 APR 6.7	DEU 49.8 APR 29.5 [*P* < 0.0001]	DEU 17.1 APR 7.9 [*P* = 0.0004]	DEU 59.0 APR 41.6 [*P* = 0.0003]	DEU 41.4 APR 21.5 [*P* < 0.0001]	N/A

Abbreviations: APR, apremilast; DEU, deucravacitinib; DLQI, Dermatology Life Quality Index; PASI, Psoriasis Area and Severity Index; PGA-F, Physician Global Assessment of Fingernails; PBO, placebo; sPGA, static Physician Global Assessment; ss-PGA, scalp-specific Physician Global Assessment.

https://doi.org/10.2147/TCRM.S388324 DovePress

Table 2 Risk-Bias Assessment of Included Studies

Ref	1. Did the Study Address a Clearly Focused Research Question?	2. Was the Assignment of Participants to Interventions Randomized?	3. Were All Participants Who Entered the Study Accounted for at Its Conclusion?	4. Were the Participants / Investigators / Assessors "Blind" to the Intervention They Were Given / Giving / Assessing?	5. Were the Study Groups Similar at the Start of the Randomized Controlled Trial?	6. Apart from the Experimental Intervention, Did Each Study Group Receive the Same Level of Care?	7. Were the Effects of Intervention Reported Comprehensively?	8. Was the Precision of the Estimate of the Intervention or Treatment Effect Reported?	9. Do the Benefits of the Experimental Intervention Outweigh the Harms and Costs?	10. Can the Results be Applied to Your Local Population / in Your Context?	11. Would the Experimental Intervention Provide Greater Value to the People in Your Care Than Any of the Existing Interventions?
Armstrong, 2023[25]	+	+	+	+	+	+	+	+	?	+	+
Papp, 2018[24]	+	+	+	+	+	+	+	+	?	+	+
Strober, 2023[26]	+	+	+	+	+	+	+	+	?	+	+

Notes: The Critical Appraisal Skills Program (CASP) checklist for randomized controlled trials was used to assess risk and bias of included studies. Each study was appraised using the checklist and was awarded (+) for Yes, (-) for No, and (?) for Cannot tell for each question on the checklist.

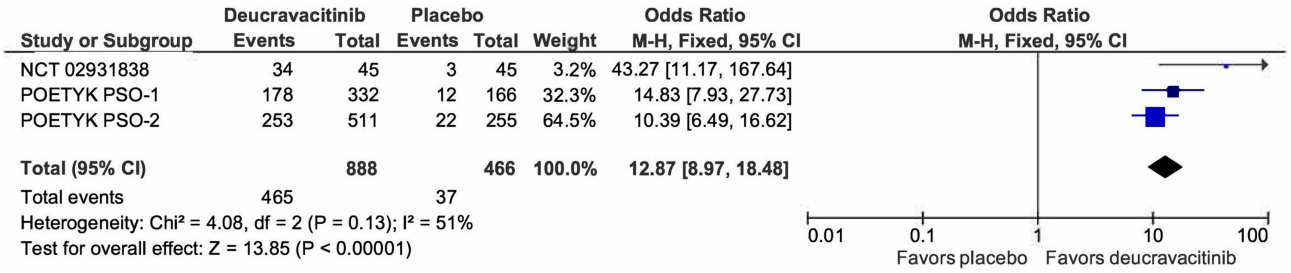

Figure 2 Forest plot of deucravacitinib versus placebo in the treatment of moderate-to-severe psoriasis. The primary outcome assessed was achievement of static Physician Global Assessment (sPGA) 0 or 1 at Week 12 (NCT02931838) or Week 16 (POETYK trials) in deucravacitinib- versus placebo-treated patients.
Abbreviations: CI, confidence interval; df, degrees of freedom; M-H, Mantel-Haenszel fixed-effects method.

12.7%) and 53.6% (vs 40.2%, 9.4%), respectively. The percent of patients who achieved sPGA 0/1 in PSO-1 and PSO-2 (vs apremilast, placebo) were 53.6% (vs 32.1%, 7.2%) and 50.3% (34.3%, 8.6%), respectively.

Safety Outcomes of Included Studies

In all included studies, deucravacitinib was well-tolerated, with similar percentages and types of adverse events (AEs) reported among patients treated with placebo or comparator drugs at Week 12 or 16.[24–26] The occurrence of any AE by Week 12 or 16 in NCT02931838, POETYK PSO-1, and POETYK PSO-2 were 64% (vs 51% in placebo group), 53.0% (vs 42.4% in placebo group, 55.4% in apremilast group), and 57.5% (vs 54.3% in placebo group, 59.1% in apremilast group), respectively. In all trials, the most frequently reported AEs associated with deucravacitinib were nasopharyngitis (6.3–11%) and upper respiratory tract infection (2–6.3%). Other common AEs reported in the POETYK trials included headache (4.3–4.8% vs 3.0–5.5% in placebo group vs 10.1–11.0% in apremilast group), diarrhea (3.9–4.7% vs 3.6–7.5% in placebo group vs 10.1–13.0% in apremilast group), and nausea (1.2–2.1% vs 1.4–2.4% in placebo group vs 9.1–11.3% in apremilast group), which occurred at similar frequencies to placebo and generally decreased frequencies compared to the apremilast treatment group. Across the three studies, no significant changes in mean blood counts (including neutrophil and platelet levels), serum lipids (including total cholesterol), creatinine, creatine phosphokinase, liver enzymes, or immunoglobulins were reported. Among all patients treated with deucravacitinib, no serious cases of herpes zoster leading to discontinuation occurred; additionally, no opportunistic infections or tuberculosis were reported.

Meta-Analysis Results

Meta-analysis of the three placebo-controlled RCTs comparing the rates of clearance (sPGA 0/1) in patients with moderate-to-severe psoriasis (N = 1354; deucravacitinib, n = 888; placebo, n = 466) demonstrated superior efficacy of deucravacitinib compared to placebo (OR, 12.87; 95% confidence interval (CI), 8.97–18.48) (Figure 2). Heterogeneity was determined as significant (χ^2 = 4.08, I^2 = 51%) (Figure 2).

Discussion

Psoriasis is a systemic, immune dysregulatory condition that has a significant detrimental impact on a patient's overall health and quality of life. While a range of biologic therapies are available for the treatment of more severe disease—including agents that target TNF-α, IL-12/IL-23, IL-17, and IL-23—certain biologics can be contraindicated for individuals based on comorbid conditions, safety concerns, or insurance coverage issues. Furthermore, patients with more severe psoriasis are more likely to experience biologic failure, including the sequential failure of multiple biologics, despite adequate time attempting each agent.[28–30] Thus, there remains a need to develop new targeted therapeutics—particularly those that can act via a different mechanism of action than existing systemic agents—to treat patients with moderate-to-severe psoriasis.

While the development of psoriasis is complex and involves an interplay between multiple immune signaling pathways, JAK/STAT signaling has been shown to hold a central dysregulatory role in psoriasis pathogenesis for years.[16] The importance of such signaling in psoriasis was further emphasized after a recent study found methotrexate

to inhibit the JAK/STAT pathway as a potential secondary mechanism of action, particularly relevant in psoriatic arthritis.[31] Unfortunately, first-generation JAK inhibitors targeting JAK2 and JAK3 (eg, tofacitinib, baricitinib) experienced limited success for psoriasis as a disease indication due to safety concerns, despite effective associated clinical outcomes (eg, PASI reduction).[32,33] For example, incidence of major adverse cardiovascular events and cancer were found to be higher in tofacitinib-treated groups in a dose-dependent fashion for rheumatoid arthritis patients.[34] Thus, JAK inhibitors were previously approved only for psoriatic arthritis or for off-label use in certain psoriasis patients who had not responded to conventional systemic therapies.[33]

Deucravacitinib represents a major advancement as a first-in-class systemic therapy that differs from prior JAK inhibitors and other psoriasis biologics in several ways. First, deucravacitinib is a small molecule, meaning it can be administered by a variety of routes, including orally—as opposed to injected or infused, as many psoriasis biologics are.[35] Because of deucravacitinib's oral bioavailability and simpler dosing regimens, adherence to the intended treatment plan may be easier to achieve for patients, and access to first-line therapy for moderate-to-severe psoriasis may be expanded due to lower drug costs.[35] Additionally, small molecules may also hold a reduced risk of immunogenicity compared to biologics, which can translate to a longer period of efficacy in individual patients.[35] Finally, our systematic review of RCTs found that psoriasis patients treated with deucravacitinib did not experience major AEs at rates significantly different from patients treated with apremilast or placebo.[26,36] In our review of the three included RCTs, the most frequently reported AEs tended to occur at similar rates compared to the placebo group and at lower frequencies compared to apremilast treatment. None of the three included RCTs reported significant changes in blood count, cholesterol levels, or opportunistic infections among patients treated with deucravacitinib, which were all concerns that hampered the approval of JAK inhibitors for psoriasis treatment in the past.[37,38] Taken together, these results suggest that deucravacitinib may have favorable safety features as a selective inhibitor of TYK2 in the JAK family—although results should be interpreted with caution due to the limited follow-up periods reported. Further head-to-head comparative studies should be conducted.

The meta-analysis conducted in our study is, to our knowledge, the first performed that compares plaque psoriasis patients treated with deucravacitinib versus placebo. The results (Figure 2) indicate that the primary endpoint of sPGA 0/1, a validated tool providing a global estimate of a patient's psoriatic disease severity, was achieved significantly more frequently in deucravacitinib compared to placebo treatment groups.[18] These promising results of clinical efficacy bode well for other TYK2 inhibitors in clinical development for psoriasis, including rapsacitinib, brepocitinib, NDI-034858, and ESK-001.[33] Overall, our systematic review and meta-analysis found deucravacitinib to yield positive improvements for multiple efficacy endpoints, including clinical outcomes (eg, sPGA, PASI) and patient-reported quality of life (via DLQI).

Conclusions

Deucravacitinib is an effective, oral small molecule that possesses good efficacy and safety features, indicating its potential to serve as a first-line treatment for moderate-to-severe psoriasis. Patients with plaque psoriasis showed significant improvements in objective, disease-specific clinical parameters, with meta-analysis of Phase II and III RCTs demonstrating the superiority of deucravacitinib compared to placebo. Within individual RCTs, deucravacitinib was also found to yield increased rates of disease improvement and reduced AE incidence compared to apremilast. Thus, deucravacitinib achieved clinical efficacy while maintaining a favorable safety profile—an important barrier to prior JAK inhibitor use in psoriasis—consistent with its unique mechanism of action and selectivity for TYK2. While further studies should be conducted to evaluate the long-term safety and efficacy of deucravacitinib and compare it to existing biologics, deucravacitinib holds promising clinical utility and represents an important step forward as a first-in-class treatment option for psoriasis patients.

Abbreviations

AE, adverse event; BID, twice daily; CASP, Critical Appraisal Skills Programme; DLQI, Dermatology Life Quality Index; FDA, Food and Drug Administration; IL, interleukin; JAK, Janus kinase; PASI, Psoriasis Area and Severity Index; PGA, Physician Global Assessment; PGA-F, PGA of Fingernail Psoriasis; QD, daily; QOD, every other day; RCT, randomized controlled trial; sPGA, static PGA; ss-PGA, scalp-specific PGA; STAT, Signal Transducers and Activators of Transcription; Th17, T helper 17; TYK, tyrosine kinase.

Data Sharing Statement

All data analyzed in this systematic review can be searched in publicly available databases including PubMed and Embase.

Ethics Approval and Informed Consent

This is a review article of published studies; ethics approval was not required by our Institutional Review Board.

Consent for Publication

No identifiable patient information was included in this article.

Acknowledgments

We are thankful to all the reviewers who contributed to this article.

Author Contributions

All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this manuscript. All authors contributed to data analysis, drafting or revising the article, have agreed on the journal to which the article will be submitted, gave final approval of the version to be published, and agree to be accountable for all aspects of the work. Conception: JQJ, VR, WL. Methodology: all authors. Formal analysis and investigation: JQJ, RKS. Writing—original draft preparation: JQJ, RKS. Writing—review and editing: all authors. Supervision: WL.

Funding

This study was not funded.

Disclosure

J.Q.J. has received research grant funding from the National Psoriasis Foundation and institutional funding from the University of California, San Francisco. T.B. has received research grant funding from Novartis and Regeneron and is a principal investigator for trials sponsored by Abbvie, Castle, CorEvitas, Dermavant, Galderma, Mindera, and Pfizer. T. B. has also served as an advisor for Abbvie, Arcutis, Boehringer-Ingelheim, Bristol Myers Squibb, Janssen, Leo, Lilly, Novartis, Pfizer, Sun, and UCB. W.L. has received research grant funding from Abbvie, Amgen, Janssen, Leo, Novartis, Pfizer, Regeneron, and TRex Bio. The authors report no other conflicts of interest in this work.

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