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The efficacy and safety of tyrosine kinase 2 inhibitor deucravacitinib in the treatment of plaque psoriasis: a systematic review and meta-analysis of randomized controlled trials

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Background: Orally effective therapeutics for plaque psoriasis with improved response rates, lower toxicity and costs are needed in clinical practices. This study aims to assess the efficacy and safety of the recently approved TYK2 inhibitor deucravacitinib in adults with moderate to severe plaque psoriasis through meta-analysis.

Methods: A systematic search was performed for eligible studies using electronic databases, including PubMed, Embase, Cochrane Library, Clinical Trials, the EU Clinical Trials Register, and the International Clinical Trials Registry Platform (ICTRP). Randomized controlled trials (RCTs) comparing the efficacy and safety of deucravacitinib vs. placebo or active comparators in adult patients with plaque psoriasis were included. The effectiveness of deucravacitinib was evaluated using a 75% improvement in Psoriasis Area and Severity Index (PASI 75) from baseline and the proportion of patients achieving the static Physician's Global Assessment (sPGA) response. The secondary endpoint was the proportion of patients achieving PASI 90, PASI 100, ssPGA 0/1, and Dermatology Life Quality Index 0/1 (DLQI). The incidence of adverse events (AEs), serious AEs (SAEs), and AE-related treatment discontinuation were statistically analyzed to determine the safety of deucravacitinib.

Results: The systematic review and meta-analysis included five RCTs involving 2,198 patients with moderate to severe plaque psoriasis. Results showed that deucravacitinib was superior to placebo as well as active comparator apremilast in multiple key endpoints, including PASI 75, sPGA 0/1, PASI 90, PASI 100, DLQI 0/1 at week 16. Moreover, a durable response was seen in the two 52-week studies. Safety assessment showed that deucravacitinib was generally well tolerated, and the incidence of AEs, SAEs, and AE-related treatment discontinuation was low and balanced across groups.

Conclusion: Deucravacitinib demonstrated superior efficacy to apremilast in adult patients with moderate to severe plaque psoriasis with an acceptable safety profile and has the potential to be used as the first-line oral therapy for plaque psoriasis.

KEYWORDS

TYK2 inhibitor, deucravacitinib, psoriasis, autoimmune disease, meta-analysis

1. Introduction

Psoriasis is a chronic, relapsing, immune-mediated inflammatory skin disorder characterized by scaly, erythematous skin lesions. Psoriasis significantly reduces the patient's quality of life or even leads to disability and imposes heavy physical and mental burdens on the patients. It is estimated that around 2% of the population worldwide was affected by this disease, and the incidence and prevalence varied across nations, regions, ages, sex, and ethnicity. Generally, the disease incidence is higher in high-income countries and regions than in other places. Moreover, it was found to be more common in adults than in children, and a slight male predominance with later onset was reported in some studies (1–4). With population growth and aging, an increasing prevalence of psoriasis has been observed over time and has received continuous attention as a global public health concern over these years (2, 3).

Conventional treatments, including topical therapy, oral systematic therapy (methotrexate, Avastin, cyclosporine, etc.), and phototherapy, either had low response rates or may cause serious side effects (5). Oral Janus kinase (JAK) inhibitors (tofacitinib, baricitinib, ruxolitinib, etc.) and phosphodiesterase 4 (PDE 4) inhibitors (apremilast) provided physicians with greatly improved therapeutic options for the treatment of psoriasis than ever. However, these drugs' response rates, safety profiles, and costs still need to be optimized (6). Biologic agents (etanercept, infliximab, adalimumab, guselkumab, Risankizumab, etc.) are currently among the most effective options for the treatment of psoriasis, as has been demonstrated in multiple clinical trials and real-life studies (7-9). However, they still have apparent limitations like inconvenient drug administration routes, intolerability, variability in response rates, fading of efficacy over time, and high costs. Treatment of psoriasis is even more challenging in real-world settings, especially in vulnerable patients (pediatric and geriatric populations, etc.) or patients with other comorbidities like obesity, hypertension, hyperlipidemia, diabetes mellitus, etc. that may have a profound long-term impact on the treatment and prognosis of psoriasis (10, 11). In fact, biologics are the only systemic therapeutics approved by the European Medicines Agency for the treatment of pediatric psoriasis (11). Moreover, the chronic nature of psoriasis requires long-term treatments, which further emphasizes the financial burden on the patients and the healthcare system (12). Orally effective therapeutics for psoriasis with improved response rates, lower toxicity and costs are still needed in clinical practices (13).

Based on the positive results of two phase III randomized, double-blind clinical trials POETYK PSO-1 and POETYK PSO-2, the tyrosine kinase 2 (TYK2) allosteric inhibitor deucravacitinib was approved by the U.S. Food and Drug Administration (FDA) in September 2022 for the treatment of adults with moderate to severe plaque psoriasis (14–16). Deucravacitinib specifically targets TYK2 and efficiently blocks the signaling of IL-23, IL-12, and type I interferon (IFN), key cytokines that are believed to play a pivotal role in the pathogenesis of multiple immune-mediated diseases, including psoriasis. In the two trials, more than 1,600 patients with moderate to severe plaque psoriasis were recruited to evaluate the efficacy and safety of deucravacitinib in the treatment of plaque psoriasis compared with placebo or apremilast. Deucravacitinib showed superiority to both placebo and apremilast in primary endpoints, including PASI 75 (≥75% reduction from baseline in Psoriasis Area and Severity Index), sPGA 0/1 [static Physician's Global Assessment score of 0 (clear) or 1 (almost clear)] at week 16, and improved the patient's quality of life in both trials. For as long as 52 weeks, patients achieving PASI 75 in the deucravacitinib arm remain stable. A durable response was also seen in patients who achieved PASI 75 in the deucravacitinib arm and were rerandomized to the placebo arm for as long as >28 weeks. The incidence of AEs and SAEs was balanced across groups, and the AE-related discontinuation rate was lower in the deucravacitinib group than placebo and apremilast. Considering that patients with plaque psoriasis require long-term medication, this further emphasized its value in clinical practices.

FDA launched warnings about the increased risk of serious heartrelated events, cancer, blood clots, and death for specific pan-JAK inhibitors in December 2021, and their approved uses were limited to certain patients. However, TYK2 is a member of the JAK family. Due to the high degree of sequence homology between the JAK family kinases, selective TYK2 inhibition was challenging but necessary. The safety concerns associated with JAK inhibitors may apply to TYK2 inhibitors. Therefore, we performed a meta-analysis based on available RCTs to systematically evaluate the efficacy and safety of deucravacitinib in the treatment of plaque psoriasis and provide a reference for its clinical application.

2. Materials and methods

2.1. Study search and selection

We searched PubMed, Embase, the Cochrane Library, Clinical Trials, the EU Clinical Trials Register, and the International Clinical Trials Registry Platform (ICTRP) by using "deucravacitinib" or "Sotyktu" or "BMS986165" as search terms. EndNote X9 was used to remove the duplicate record. After removing duplicate records from the search results, two researchers screened and reviewed each study independently, and the inclusion of a study was decided by consensus between the two investigators. Any disagreement that happened in the process was resolved by consulting a third researcher. The included studies met the following criteria: patients diagnosed with psoriasis; age 18 years old; receiving deucravacitinib therapy; comparison of deucravacitinib vs. placebo or active comparators; RCT; reporting of the efficacy and safety outcomes. All the data were extracted from the included studies, including the authorship, year of publication, study design, study duration, study site, study population, interventions and comparators, clinical outcomes, and risk of AEs. Ethical approval was not required for meta-analysis in our institute.

2.2. Outcome measurement

The study's primary endpoint was the proportion of patients achieving PASI 75 or sPGA 0/1, commonly used in clinical trials targeting plaque psoriasis. The secondary endpoint was the proportion of patients achieving PASI 90, PASI 100, ssPGA 0/1, and \geq 2 score improvement of the Dermatology Life Quality Index (DLQI). The incidence of adverse events (AEs), serious AEs (SAEs), and AE-related treatment discontinuation was statistically analyzed to determine the safety of deucravacitinib.

2.3. Data analysis

The included studies' quality and associated risk of bias were performed using the Cochrane risk of bias tool (17). Two researchers subjectively reviewed all included studies and rated them "low risk," "high risk," or "unclear risk" according to the judgment items in the tool. All statistical analyses were performed using Review Manager version 5.3. Pooled odds ratios (ORs) with a 95% credibility interval (CI) were used for comparing the efficacy and safety of deucravacitinib with placebo or comparators. Study heterogeneity was presented using the Chi-squared-based Cochran's Q statistic and I2. When p < 0.10 or $I^2 > 50\%$, the heterogeneity was considered significant. The fixed-effect model was used when the data were homogenous, and the

random-effect model was used when the data were significantly heterogeneous.

3. Results

3.1. Search and study characteristics

A flow diagram of the study selection is presented in Figure 1. The search program yielded 599 references. After excluding 234 duplicates, the remaining 365 articles were screened for eligibility, and another 352 were excluded. Full-text reviews were performed for the remaining 13 articles, and five randomized controlled trials (RCTs) with 2,198 patients met the inclusion criteria and were included in the systematic review and meta-analysis. Four of the five studies were publicly published, and one clinical trial (NCT04167462) was not published but had results open to the public (14, 15, 18, 19). All five studies were placebo-controlled, conducted between 2018 and 2023 in multiple countries. In the two 52-week trials, data at the timepoint of week 16 was included for integrated analysis. Papp's study protocol consists of multiple dosing regimens, and only the group of patients taking the recommended dose of 12 mg QD was included for analysis (18). Of the 2,198 participants included, the number of patients receiving deucravacitinib 6 mg QD, deucravacitinib 12 mg QD, placebo, and active comparator apremilast was 1,059, 111, 540, and 488, respectively. 1,473 (67%) patients were male, and all were diagnosed with moderate to severe plaque psoriasis. Details of included RCTs and characteristics of the included patients are presented in Table 1.

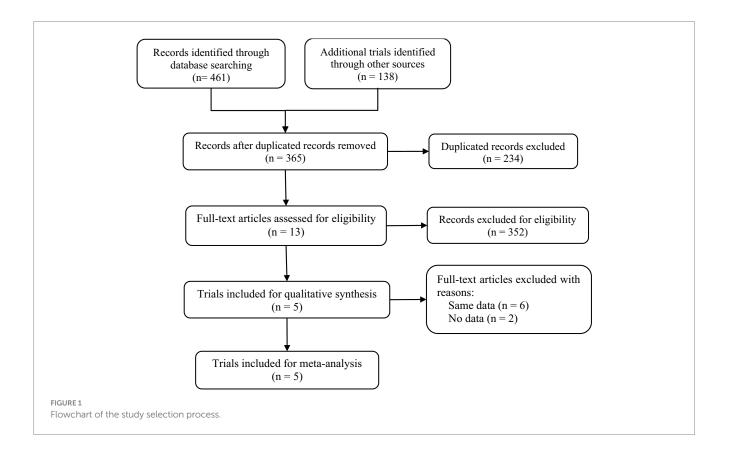


TABLE 1	Details of included	RCTs and	characteristics of	the included patients.

Study	Intervention	Therapy duration	Study population	Study design	Male (%)	Age (years), Mean <u>+</u> SD
Strober et al. (14)	6 mg QD (N = 511)	52-week	18 years and older,	Multi-Center,	336 (65.75)	46.9 ± 13.37
(NCT03611751)	Placebo (N = 255)		Plaque psoriasis for at least 6 months, Moderate to severe disease, Candidate for phototherapy or systemic therapy	Randomized,	181 (70.98)	47.3 ± 13.57
	Apremilast 30 mg BID (N = 254)			Double-Blind, Placebo—and Active Comparator— Controlled Phase 3 Study	157 (61.81)	46.4 ± 13.28
Armstrong et al. (15) (NCT03624127)	6 mg QD (N = 332)	52-week	18 years and older,	Multi-Center,	230 (69.28)	45.9 ± 13.71
	placebo (<i>N</i> = 166)		Plaque psoriasis for at	Randomized, Double-Blind, Placebo—and Active Comparator— Controlled Phase 3 Study	113 (68.07)	47.9 ± 13.98
	Apremilast 30 mg BID (N = 168)		least 6 months, Moderate to severe disease, Candidate for phototherapy or systemic therapy		110 (65.48)	44.7 ± 12.06
NCT04167462	6 mg QD (N = 146)	16-week	18 years and older,	Multi-Center,	123 (84.2)	40.3 ± 12.19
	Placebo (<i>N</i> = 74)		Plaque psoriasis for at least 6 months, Moderate to severe disease, Candidate for phototherapy or systemic therapy	Randomized, Double-Blind, Placebo-Controlled Phase 3 Study	57 (77.0)	41.2 ± 12.33
Papp et al. (18)	$12 \mathrm{mg} \mathrm{QD} (N = 44)$	12-week	18 years and older,	Randomized, double-	30 (68.18)	46.6 ± 11.62
(NCT02931838)	Placebo (N = 45)		Plaque psoriasis for at least 6 months, Moderate to severe disease, body-mass index of 18 to 40, Candidate for phototherapy or systemic therapy	blind, placebo- controlled, phase 2 trial	37 (82.22)	46.4 ± 11.93
Mease et al. (19)	6 mg QD (N = 70)	16-week	18 years and older,	Randomized, double-	40 (57.14)	50.5 ± 13.69
NCT03881059)	$12 \mathrm{mg} \mathrm{QD} (N = 67)$		Plaque psoriasis for at least 6 months,	blind, phase 2,	33 (49.25)	50.5 ± 13.75
	Placebo (<i>N</i> = 66)			placebo-controlled	26 (39.39)	48.5 ± 13.17

According to the Cochrane Collaboration tool for assessing the risk of bias, all included trials were classified as having a low risk of bias and eligible for meta-analysis. Details of bias assessment are shown in Figures 2, 3.

3.2. The efficacy and safety of deucravacitinib for plaque psoriasis

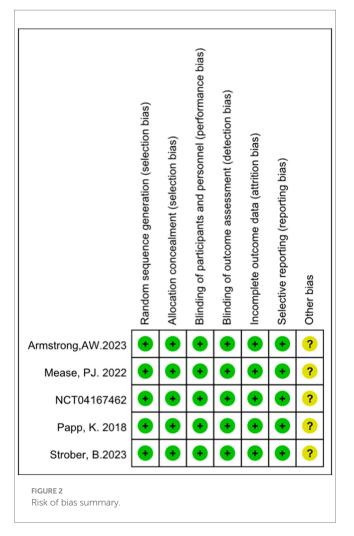
3.2.1. Efficacy

The efficacy data extracted from the included studies are presented below. All five studies reported the outcome of PASI75: four studies compared deucravacitinib (6 mg) vs. placebo, two studies compared deucravacitinib (12 mg) vs. placebo, and two studies compared the deucravacitinib (6 mg) vs. apremilast. According to the results, the proportion of patients achieving PASI75 was significantly higher in the deucravacitinib arm (6 mg) than placebo (Figure 4A, 56.2% vs. 11.4%, OR=9.82, 95% CI=7.36–13.11, I^2 =77%) and active comparator apremilast (Figure 4A, 55.2% vs. 37.9%, OR=2.01, 95% CI=1.58–2.55, I^2 =64%). A higher dose of deucravacitinib (12 mg) was associated with a further improved PASI75 rate over placebo (Figure 4A, 65.8% vs. 14.4%, OR=10.47, 95% CI=5.48–19.99, I^2 =83%).

The same superiority was also observed in the other primary endpoint s-PGA 0/1. Four studies reported the outcome of s-PGA 0/1. Results showed that patients receiving deucravacitinib (6 mg) had a higher response rate than placebo (Figure 4B, 51.8% vs. 7.88%, OR = 12.50, 95% CI = 8.81–17.73, I^2 = 0%) and apremilast (Figure 4B, 51.1% vs. 33.2%, OR = 2.11, 95% CI = 1.65–2.69, I^2 = 0%). Only one study reported the outcome of s-PGA 0/1 comparing deucravacitinib

(12 mg) vs. placebo, and a better efficacy was also observed (Figure 4B, 75.0% vs. 6.67%, OR = 42.00, 95% CI = 10.83–162.92), though with a relatively small sample size (N=89).

Patients receiving deucravacitinib (6 mg) treatment had a significantly higher PASI90 response rate over placebo (Figure 5A, 31.5% vs. 3.03%, OR = 14.79) and apremilast (Figure 5A, 30.4% vs. 18.8%, OR = 1.90). A similar predominance was also observed for the

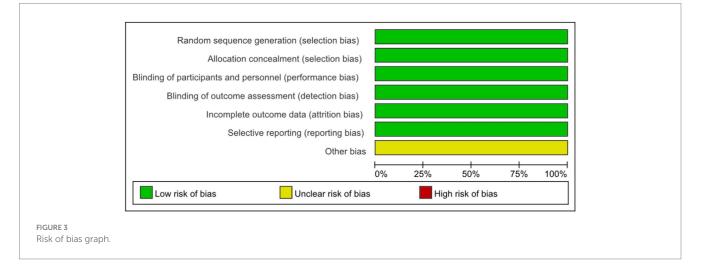


PASI100 response rate (Figure 5B, 10.6% vs. 0.81%, OR=12.99 vs. placebo; 11.7% vs. 3.79%, OR=3.37 vs. apremilast). A higher dosage of deucravacitinib (12 mg) results in simultaneously increased PASI90 (Figure 5A, 43.2%) and PASI100 (Figure 5B, 25.0%) response rates. Moreover, the proportion of patients achieving ss-PGA 0/1 (Figure 6A, 63.8% vs. 16.2%, OR=9.17, vs. placebo; 37.7% vs. 17.3%, OR=2.88, vs. apremilast) and DLQI 0/1 (Figure 6B, 41.6% vs. 10.1%, OR=6.37, vs. placebo; 38.9% vs. 25.2%, OR=1.89, vs. apremilast) in the deucravacitinib (6 mg) group was significantly higher than placebo and apremilast.

3.2.2. Safety

The safety of deucravacitinib is a significant concern for supervisors, physicians, and patients due to the emerging serious side effects of JAK inhibitors. In this research, the incidence of AEs, SAEs, and AE-related treatment discontinuation rates were statistically analyzed. Due to the mechanism of action of deucravacitinib, nasopharyngitis and upper respiratory tract infection were the most common AEs reported in deucravacitinib-treated patients. The proportion of patients with nasopharyngitis in the deucravacitinib (6 mg) group was comparable to that of placebo (Figure 7A, 8.50% vs. 8.19%, OR=1.03) and apremilast (Figure 7A, 9.02% vs. 8.77%, OR = 1.03). A higher dosage of deucravacitinib (12 mg) results in a slightly increased incidence of nasopharyngitis over placebo (Figure 7A, 12.6% vs. 6.31%, OR = 2.15). The occurrence of upper respiratory tract infection in the deucravacitinib (6 mg) group was slightly higher than in placebo (Figure 7B, 7.18% vs. 3.74%, OR = 1.91) and apremilast (Figure 7B, 5.46% vs. 4.03%, OR=1.37). Nausea (Figure 7C, 1.66% vs. 1.66%, OR = 1.00, vs. placebo; 1.66% vs. 9.95%, OR=0.15, vs. apremilast), diarrhea (Figure 7D, 4.71% vs. 4.52%, OR = 1.06, vs. placebo; 4.51% vs. 10.66%, OR = 0.40, vs. apremilast), and headache (Figure 7E, 4.82% vs. 4.63%, OR=1.06, vs. placebo; 4.51% vs. 10.66%, OR = 0.40, vs. apremilast) were the other side effects reported with high frequency, but analysis showed that they were more common in the apremilast group than deucravacitinib and placebo. Generally, the incidence of AEs across groups was low, and the symptoms were mild and usually resolved without treatment.

Low and balanced rates of SAEs were reported across groups: the incidence of SAEs in the deucravacitinib (6 mg) group was less than that of placebo (Figure 7F, 1.79% vs. 2.50%, OR = 0.69) but a bit more



Study or Subaroup	Experime Events		Contr Events		Weight	Odds Ratio M-H, Fixed, 95% CI	Odds Ratio M-H. Fixed, 95% Cl
1.1.1 Deucravacitinib					-		
Armstrong,AW.2023	194	332	21	166	8.4%	9.71 [5.85, 16.12]	
Mease, PJ. 2022	30	70	13	66	5.5%	3.06 [1.42, 6.60]	
NCT04167462	99	144	6	7∠	1.8%	24.93 [10.08, 61.70]	
Strober, B.2023	271	511	24	255	10.8%	10.87 [6.90, 17.13]	
Subtotal (95% CI)		1057		561	26.5%	9.82 [7.36, 13.11]	•
Total events	594		64				
Heterogeneity: Chi ² = Test for overall effect:				= 77%			
1.1.2 Deucravacitinib	12mg vs p	olacebo					
Mease, PJ. 2022	40	67	13	66	3.8%	6.04 [2.77, 13.16]	
Papp, K. 2018	33	44	3	45		42.00 [10.83, 162.92]	
Subtotal (95% CI)		111		111	4.3%	10.47 [5.48, 19.99]	•
Total events	73		16				
Heterogeneity: Chi ² = Test for overall effect:				3%			
1.1.3 Deucravacitinib	vs Aprem	ilast					
Armstrong,AW.2023	194	332	59	168	23.5%	2.60 [1.77, 3.82]	
Strober, B.2023	271	511	101	254	45.7%	1.71 [1.26, 2.32]	
Subtotal (95% CI)		843		422	69.1%	2.01 [1.58, 2.55]	
Total events	465		160				
Heterogeneity: Chi ² = Test for overall effect:	,			4%			
Total (95% CI)		2011		1094	100.0%	4.45 [3.76, 5.27]	◆
Total events	1132		240				
Heterogeneity: Chi ² =	94.99, df =	7 (P < 0	.00001); I	² = 93 ⁰	%		
Test for overall effect:	7 = 17.38 (001				0.01 0.1 1 10 10
	2 - 17.00 (F > 0.00	JUU I)				Fourier four entrell Fourier foontall
Test for subaroup diffe	```		,	(P < 0.	00001). F	² = 97.4%	Favours [experimental] Favours [control]
Test for subaroup diffe	erences: Ch	i² = 77.6	60. df = 2		00001). F		
	erences: Ch Experime	i² = 77.6 ental	0. df = 2 Contr	ol		Odds Ratio	Odds Ratio
Study or Subgroup	erences: Ch Experime Events	i² = 77.6 ental Total	0. df = 2 Contr	ol			Odds Ratio
<u>Study or Subgroup</u> 1.2.1 Deucravacitinik	Experime Experime Events 6 6mg vs pl	i² = 77.6 ental <u>Total</u> acebo	60. df = 2 Contr Events	ol Total	Weight	Odds Ratio M-H. Fixed. 95% CI	Odds Ratio
Study or Subgroup 1.2.1 Deucravacitinik Armstrong,AW.2023	erences: Ch Experim Events 6 6mg vs pl 178	i ² = 77.6 ental <u>Total</u> acebo 332	60. df = 2 Contr Events 12	ol <u>Total</u> 166	Weight 6.3%	Odds Ratio M-H. Fixed. 95% CI 14.83 [7.93, 27.73]	Odds Ratio
<u>Study or Subgroup</u> 1.2.1 Deucravacitinik Armstrong,AW.2023 NCT04167462	erences: Ch Experime Events o 6mg vs pl 178 80	i ² = 77.6 ental Total acebo 332 144	30. df = 2 Contr <u>Events</u> 12 5	ol <u>Total</u> 166 74	Weight 6.3% 2.5%	Odds Ratio <u>M-H, Fixed, 95% CI</u> 14.83 [7.93, 27.73] 17.25 [6.57, 45.30]	Odds Ratio
Study or Subgroup 1.2.1 Deucravacitinik Armstrong,AW.2023 NCT04167462 Strober, B.2023	erences: Ch Experim Events 6 6mg vs pl 178	i ² = 77.6 ental <u>Total</u> acebo 332	60. df = 2 Contr Events 12	ol <u>Total</u> 166	Weight 6.3% 2.5% 12.6%	Odds Ratio M-H. Fixed. 95% Cl 14.83 (7.93, 27.73) 17.25 (6.57, 45.30) 10.39 (6.49, 16.62)	Odds Ratio
Study or Subgroup 1.2.1 Deucravacitinik Armstrong,AW.2023 NCT04167462 Strober, B.2023 Subtotal (95% CI)	erences: Ch Experime Events 9 6mg vs pl 178 80 253	i ² = 77.6 ental Total acebo 332 144 511	30. df = 2 Contr <u>Events</u> 12 5	ol <u>Total</u> 166 74 255	Weight 6.3% 2.5%	Odds Ratio <u>M-H, Fixed, 95% CI</u> 14.83 [7.93, 27.73] 17.25 [6.57, 45.30]	Odds Ratio
Study or Subgroup 1.2.1 Deucravacitinik Armstrong,AW.2023 NCT04167462 Strober, B.2023	erences: Ch Experime Events o 6mg vs pl 178 80 253 511 1.31, df = 2	i ² = 77.6 ental Total acebo 332 144 511 987 (P = 0.5	50. df = 2 Contr Events 12 5 22 39 52); l ² = 0	ol <u>Total</u> 166 74 255 495	Weight 6.3% 2.5% 12.6%	Odds Ratio M-H. Fixed. 95% Cl 14.83 (7.93, 27.73) 17.25 (6.57, 45.30) 10.39 (6.49, 16.62)	Odds Ratio
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Study or Subgroup 1.2.1 Deucravacitinik Armstrong,AW.2023 NCT04167462 Strober, B.2023 Subtotal (95% CI) Total events Heterogeneity: Chi ² = Test for overall effect: 1.2.2 Deucravacitinik	Experime Events 6 6mg vs pl 178 80 253 511 1.31, df = 2 Z = 14.16 (12mg vs p	i ² = 77.6 ental <u>Total</u> acebo 332 144 511 987 (P = 0.9 P < 0.00 Diacebo	50. df = 2 Contr Events 12 5 22 39 52); l ² = 0 0001)	ol <u>Total</u> 166 74 255 495 %	Weight 6.3% 2.5% 12.6% 21.5%	Odds Ratio M-H. Fixed, 95% Cl 14.83 (7.93, 27.73) 17.25 [6.57, 45.30] 10.39 [6.49, 16.62] 12.50 [8.81, 17.73]	Odds Ratio
Study or Subgroup 1.2.1 Deucravacitinik Armstrong,AW.2023 NCT04167462 Strober, B.2023 Subtotal (95% Cl) Total events Heterogeneity: Chi ² = Test for overall effect:	Experime Events b 6mg vs pl 178 80 253 511 1.31, df = 2 Z = 14.16 (i ² = 77.6 ental Total acebo 332 144 511 987 (P = 0.3 P < 0.00	30. df = 2 Contr Events 12 5 22 39 52); I² = 0 0001)	ol <u>Total</u> 166 74 255 495	Weight 6.3% 2.5% 12.6% 21.5%	Odds Ratio M-H. Fixed. 95% Cl 14.83 (7.93, 27.73) 17.25 (6.57, 45.30) 10.39 (6.49, 16.62)	Odds Ratio
Study or Subgroup 1.2.1 Deucravacitinik Armstrong,AW.2023 NCT04167462 Strober, B.2023 Subtotal (95% CI) Total events Heterogeneity: Chi ² = Test for overall effect: 1.2.2 Deucravacitinik Papp, K. 2018 Subtotal (95% CI)	Experime Events 0 6mg vs pl 178 80 253 511 1.31, df = 2 Z = 14.16 (0 12mg vs p 33	i ² = 77.6 ental <u>Total</u> acebo 332 144 511 987 (P = 0.9 P < 0.00 Dlacebo 44	50. df = 2 Contr Events 12 5 22 39 52); l ² = 0 0001) 3	ol <u>Total</u> 166 74 255 495 %	Weight 6.3% 2.5% 12.6% 21.5%	Odds Ratio M-H. Fixed. 95% CI 14.83 (7.93, 27.73) 17.25 (6.57, 45.30) 10.39 (6.49, 16.62) 12.50 [8.81, 17.73] 42.00 [10.83, 162.92]	Odds Ratio
Study or Subgroup 1.2.1 Deucravacitinik Armstrong,AW.2023 NCT04167462 Strober, B.2023 Subtotal (95% CI) Total events Heterogeneity: Chi ² = Test for overall effect: 1.2.2 Deucravacitinik Papp, K. 2018	erences: Ch Experime Events o 6mg vs pl 178 80 253 511 1.31, df = 2 Z = 14.16 (0 12mg vs p 33 33 plicable	i ² = 77.6 ental <u>Total</u> acebo 332 144 511 987 (P = 0.9 P < 0.00 blacebo 44 44	50. df = 2 Contr Events 12 5 22 39 52); l ² = 0 0001) 3 3	ol <u>Total</u> 166 74 255 495 %	Weight 6.3% 2.5% 12.6% 21.5%	Odds Ratio M-H. Fixed. 95% CI 14.83 (7.93, 27.73) 17.25 (6.57, 45.30) 10.39 (6.49, 16.62) 12.50 [8.81, 17.73] 42.00 [10.83, 162.92]	Odds Ratio
Study or Subgroup 1.2.1 Deucravacitinik Armstrong,AW.2023 NCT04167462 Strober, B.2023 Subtotal (95% CI) Total events Heterogeneity: Chi ² = Test for overall effect: 1.2.2 Deucravacitinik Papp, K. 2018 Subtotal (95% CI) Total events Heterogeneity: Not ap Test for overall effect:	Experime Events 6 6mg vs pl 178 80 253 511 1.31, df = 2 Z = 14.16 (12mg vs p 33 33 plicable Z = 5.40 (P	$i^2 = 77.6$ ental Total acebo 332 144 511 987 (P = 0.9 P < 0.00 0lacebo 44 44	50. df = 2 Contr Events 12 5 22 39 52); l ² = 0 0001) 3 3	ol <u>Total</u> 166 74 255 495 %	Weight 6.3% 2.5% 12.6% 21.5%	Odds Ratio M-H. Fixed. 95% CI 14.83 (7.93, 27.73) 17.25 (6.57, 45.30) 10.39 (6.49, 16.62) 12.50 [8.81, 17.73] 42.00 [10.83, 162.92]	Odds Ratio
Study or Subgroup 1.2.1 Deucravacitinik Armstrong,AW.2023 NCT04167462 Strober, B.2023 Subtotal (95% CI) Total events Heterogeneity: Chi ² = Test for overall effect: 1.2.2 Deucravacitinik Papp, K. 2018 Subtotal (95% CI) Total events Heterogeneity: Not ap Test for overall effect: 1.2.3 Deucravacitinik	erences: Ch Experime 5 6mg vs pl 178 80 253 511 1.31, df = 2 Z = 14.16 (12mg vs p 33 plicable Z = 5.40 (P vs Aprem	$i^2 = 77.6$ ental Total acebo 332 144 511 987 (P = 0.9 P < 0.00 blacebo 44 44	30. df = 2 Contr Events 12 5 22 39 52); l ² = 0 0001) 3 3 3 001)	ol Total 166 74 255 495 %	Weight 6.3% 2.5% 12.6% 21.5% 0.6% 0.6%	Odds Ratio M-H, Fixed, 95% Cl 14.83 [7.93, 27.73] 17.25 [6.57, 45.30] 10.39 [6.49, 16.62] 12.50 [8.81, 17.73] 42.00 [10.83, 162.92] 42.00 [10.83, 162.92]	Odds Ratio
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Study or Subgroup 1.2.1 Deucravacitinik Armstrong,AW.2023 NCT04167462 Strober, B.2023 Subtotal (95% CI) Total events Heterogeneity: Chi ² = Test for overall effect: 1.2.2 Deucravacitinik Papp, K. 2018 Subtotal (95% CI) Total events Heterogeneity: Not ap Test for overall effect: 1.2.3 Deucravacitinik Armstrong,AW.2023 Strober, B.2023 Subtotal (95% CI)	erences: Ch Experime Events 0 6mg vs pl $178 \\ 80 \\ 253 \\ 511 \\ 1.31, df = 2 \\ Z = 14.16 (10) \\ 0 \text{ 12mg vs p} \\ 33 \\ 33 \\ 0 \text{ plicable} \\ Z = 5.40 (P) \\ 0 \text{ vs Aprem} \\ 178 \\ 253 \\ 253 \\ 0 \text{ vs Aprem} \\ 178 \\ 253 \\ 0 \text{ vs Aprem} \\ 178 \\ 253 \\ 0 \text{ vs Aprem} \\ 178 \\ 253 \\ 0 \text{ vs Aprem} \\ 0 \text{ vs Aprem} \\ 178 \\ 253 \\ 0 \text{ vs Aprem} \\ 0 vs Apr$	$i^2 = 77.6$ ental Total acebo 332 144 511 987 (P = 0.3 P < 0.00 blacebo 44 44 c < 0.000 ilast 332 511	50. df = 2 Contr Events 12 5 22 39 52); l ² = 0 0001) 3 3 001) 54 86	ol <u>Total</u> 166 74 255 495 % 45 45 45	Weight 6.3% 2.5% 12.6% 21.5% 0.6% 0.6% 0.6% 28.4% 49.5%	Odds Ratio M-H. Fixed. 95% CI 14.83 (7.93, 27.73) 17.25 (6.57, 45.30) 10.39 (6.49, 16.62) 12.50 [8.81, 17.73] 42.00 [10.83, 162.92] 42.00 [10.83, 162.92] 42.00 [10.83, 162.92]	Odds Ratio
Study or Subgroup 1.2.1 Deucravacitinik Armstrong,AW.2023 NCT04167462 Strober, B.2023 Subtotal (95% CI) Total events Heterogeneity: Chi ² = Test for overall effect: 1.2.2 Deucravacitinik Papp, K. 2018 Subtotal (95% CI) Total events Heterogeneity: Not ap Test for overall effect: 1.2.3 Deucravacitinik Armstrong,AW.2023 Strober, B.2023	erences: Ch Experime Fevents 6 Gmg vs pl 178 80 253 511 1.31, df = 2 Z = 14.16 (12mg vs p 33 33 plicable Z = 5.40 (P vs Aprem 178 253 431 0.90, df = 1	$i^2 = 77.6$ ental Total acebo 332 144 511 987 (P = 0.9 P < 0.00 44 44 44 2 < 0.000 ilast 332 511 843 (P = 0.3	50. df = 2 Contr Events 12 5 22 39 52); l ² = 0 0001) 3 3 001) 54 86 140 34); l ² = 0	ol Total 166 74 255 495 % 45 45 45 45 168 254 422	Weight 6.3% 2.5% 12.6% 21.5% 0.6% 0.6% 0.6% 28.4% 49.5%	Odds Ratio M-H. Fixed. 95% CI 14.83 (7.93, 27.73) 17.25 (6.57, 45.30) 10.39 (6.49, 16.62) 12.50 [8.81, 17.73] 42.00 [10.83, 162.92] 42.00 [10.83, 162.92] 42.00 [10.83, 162.92]	Odds Ratio
Study or Subgroup 1.2.1 Deucravacitinik Armstrong,AW.2023 NCT04167462 Strober, B.2023 Subtotal (95% Cl) Total events Heterogeneity: Chi ² = Test for overall effect: 1.2.2 Deucravacitinik Papp, K. 2018 Subtotal (95% Cl) Total events Heterogeneity: Not ap Test for overall effect: 1.2.3 Deucravacitinik Armstrong,AW.2023 Strober, B.2023 Subtotal (95% Cl) Total events Heterogeneity: Chi ² =	erences: Ch Experime Fevents 6 Gmg vs pl 178 80 253 511 1.31, df = 2 Z = 14.16 (12mg vs p 33 33 plicable Z = 5.40 (P vs Aprem 178 253 431 0.90, df = 1	$i^2 = 77.6$ ental Total acebo 332 144 511 987 (P = 0.9 P < 0.00 44 44 44 2 < 0.000 ilast 332 511 843 (P = 0.3	50. df = 2 Contr Events 12 5 22 39 52); l ² = 0 0001) 3 3 001) 54 86 140 34); l ² = 0	ol Total 166 74 255 495 % 45 45 45 168 254 422 %	Weight 6.3% 2.5% 12.6% 21.5% 0.6% 0.6% 0.6% 28.4% 49.5%	Odds Ratio M-H. Fixed. 95% CI 14.83 (7.93, 27.73) 17.25 (6.57, 45.30) 10.39 (6.49, 16.62) 12.50 [8.81, 17.73] 42.00 [10.83, 162.92] 42.00 [10.83, 162.92] 42.00 [10.83, 162.92]	Odds Ratio
Study or Subgroup 1.2.1 Deucravacitinik Armstrong,AW.2023 NCT04167462 Strober, B.2023 Subtotal (95% Cl) Total events Heterogeneity: Chi ² = Test for overall effect: 1.2.2 Deucravacitinik Papp, K. 2018 Subtotal (95% Cl) Total events Heterogeneity: Not ap Test for overall effect: 1.2.3 Deucravacitinik Armstrong,AW.2023 Strober, B.2023 Subtotal (95% Cl) Total events Heterogeneity: Chi ² = Test for overall effect:	erences: Ch Experime Fevents 6 Gmg vs pl 178 80 253 511 1.31, df = 2 Z = 14.16 (12mg vs p 33 33 plicable Z = 5.40 (P vs Aprem 178 253 431 0.90, df = 1	$i^2 = 77.6$ ental Total acebo 332 144 511 987 (P = 0.3 P < 0.00 0lacebo 44 44 c < 0.000 ilast 332 511 843 (P = 0.3 c < 0.000	50. df = 2 Contr Events 12 5 22 39 52); l ² = 0 0001) 3 3 001) 54 86 140 34); l ² = 0	ol Total 166 74 255 495 % 45 45 45 168 254 422 %	Weight 6.3% 2.5% 12.6% 21.5% 0.6% 0.6% 49.5% 77.9%	Odds Ratio M-H. Fixed. 95% Cl 14.83 (7.93, 27.73) 17.25 (6.57, 45.30) 10.39 (6.49, 16.62) 12.50 [8.81, 17.73] 42.00 [10.83, 162.92] 42.00 [10.83, 162.92] 42.00 [10.83, 162.92] 2.44 [1.65, 3.60] 1.92 [1.40, 2.62] 2.11 [1.65, 2.69]	Odds Ratio
Study or Subgroup 1.2.1 Deucravacitinik Armstrong,AW.2023 NCT04167462 Strober, B.2023 Subtotal (95% Cl) Total events Heterogeneity: Chi ² = Test for overall effect: 1.2.2 Deucravacitinik Papp, K. 2018 Subtotal (95% Cl) Total events Heterogeneity: Not ap Test for overall effect: 1.2.3 Deucravacitinik Armstrong,AW.2023 Subtotal (95% Cl) Total events Heterogeneity: Chi ² = Test for overall effect: Total (95% Cl) Total events Heterogeneity: Chi ² =	erences: Ch Experime Events 0 6mg vs pl 178 80 253 511 1.31, df = 2 Z = 14.16 (0 12mg vs p 33 33 plicable Z = 5.40 (P 0 vs Aprem 178 253 431 0.90, df = 1 Z = 6.00 (P 975 82.74, df =	$i^2 = 77.6$ ental Total acebo 332 144 511 987 (P = 0.3 P < 0.00 41 44 2 < 0.000 illast 332 511 843 (P = 0.3 -511 843 (P = 0.3 -511 843 (P = 0.3 -511 -843 (P = 0.3 -511 -874 -511 -874 -511 -874 -511 -874 -511 -874 -511 -874 -511 -874 -511 -874 -511 -874 -511 -874 -511 -874 -511 -874 -511 -874 -511 -874 -511 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774	So. df = 2 Contr Events 12 5 22 39 52); $l^2 = 0$ 0001) 3 3 001) 54 86 140 34); $l^2 = 0$ 001) 182 .00001); l^2	ol Total 166 74 255 495 % 45 45 45 168 254 422 % 962	Weight 6.3% 2.5% 12.6% 21.5% 0.6% 0.6% 49.5% 77.9%	Odds Ratio M-H. Fixed. 95% Cl 14.83 (7.93, 27.73) 17.25 (6.57, 45.30) 10.39 (6.49, 16.62) 12.50 [8.81, 17.73] 42.00 [10.83, 162.92] 42.00 [10.83, 162.92] 42.00 [10.83, 162.92] 2.44 [1.65, 3.60] 1.92 [1.40, 2.62] 2.11 [1.65, 2.69]	Odds Ratio M-H, Fixed. 95% Cl
Study or Subgroup 1.2.1 Deucravacitinik Armstrong,AW.2023 NCT04167462 Strober, B.2023 Subtotal (95% CI) Total events Heterogeneity: Chi ² = Test for overall effect: 1.2.2 Deucravacitinik Papp, K. 2018 Subtotal (95% CI) Total events Heterogeneity: Not ap Test for overall effect: 1.2.3 Deucravacitinik Armstrong,AW.2023 Strober, B.2023 Subtotal (95% CI) Total events Heterogeneity: Chi ² = Test for overall effect: Total (95% CI) Total events	erences: Ch Experime Events 0 6mg vs pl 178 80 253 511 1.31, df = 2 Z = 14.16 (0 12mg vs p 33 33 plicable Z = 5.40 (P 0 vs Aprem 178 253 431 0.90, df = 1 Z = 6.00 (P 975 82.74, df =	$i^2 = 77.6$ ental Total acebo 332 144 511 987 (P = 0.3 P < 0.00 41 44 2 < 0.000 illast 332 511 843 (P = 0.3 -511 843 (P = 0.3 -511 843 (P = 0.3 -511 -843 (P = 0.3 -511 -874 -511 -874 -511 -874 -511 -874 -511 -874 -511 -874 -511 -874 -511 -874 -511 -874 -511 -874 -511 -874 -511 -874 -511 -874 -511 -874 -511 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774 -774	So. df = 2 Contr Events 12 5 22 39 52); $l^2 = 0$ 0001) 3 3 001) 54 86 140 34); $l^2 = 0$ 001) 182 .00001); l^2	ol Total 166 74 255 495 % 45 45 45 168 254 422 % 962	Weight 6.3% 2.5% 12.6% 21.5% 0.6% 0.6% 49.5% 77.9%	Odds Ratio M-H. Fixed. 95% Cl 14.83 (7.93, 27.73) 17.25 (6.57, 45.30) 10.39 (6.49, 16.62) 12.50 [8.81, 17.73] 42.00 [10.83, 162.92] 42.00 [10.83, 162.92] 42.00 [10.83, 162.92] 2.44 [1.65, 3.60] 1.92 [1.40, 2.62] 2.11 [1.65, 2.69]	Odds Ratio M-H, Fixed, 95% Cl
Study or Subgroup 1.2.1 Deucravacitinik Armstrong,AW.2023 NCT04167462 Strober, B.2023 Subtotal (95% Cl) Total events Heterogeneity: Chi ² = Test for overall effect: 1.2.2 Deucravacitinik Papp, K. 2018 Subtotal (95% Cl) Total events Heterogeneity: Not ap Test for overall effect: 1.2.3 Deucravacitinik Armstrong,AW.2023 Subtotal (95% Cl) Total events Heterogeneity: Chi ² = Test for overall effect: Total (95% Cl) Total events Heterogeneity: Chi ² =	Prences: Ch Experime Events 0 6mg vs pl 178 80 253 511 1.31, df = 2 Z = 14.16 (0 12mg vs p 33 plicable Z = 5.40 (P 0 vs Aprem 178 253 431 0.90, df = 1 Z = 6.00 (P 975 82.74, df = Z = 16.11 (i ² = 77.6 ental Total acebo 332 144 511 987 (P = 0.9 P < 0.00 6 ilast 332 511 843 (P = 0.3 511 843 (P = 0.3 511 843 (P = 0.3 511 843	So. df = 2 Contr Events 12 5 22 39 52); $l^2 = 0$ 0001) 3 3 001) 54 86 140 34); $l^2 = 0$ 001) 182 100001); l^2	ol Total 166 74 255 495 % 45 45 45 45 45 45 45 45 45 45 45 45 45	Weight 6.3% 2.5% 12.6% 21.5% 0.6% 0.6% 49.5% 77.9% 100.0%	Odds Ratio M-H. Fixed, 95% Cl 14.83 (7.93, 27.73) 17.25 [6.57, 45.30] 10.39 [6.49, 16.62] 12.50 [8.81, 17.73] 42.00 [10.83, 162.92] 42.00 [10.83, 162.92] 42.00 [10.83, 162.92] 2.44 [1.65, 3.60] 1.92 [1.40, 2.62] 2.11 [1.65, 2.69] 4.59 [3.81, 5.53]	Odds Ratio M-H, Fixed. 95% Cl

than the apremilast group (Figure 7F, 1.78% vs. 1.18%, OR = 1.52). Infection was the most frequently reported SAE, as has been seen with other immunomodulatory agents. Most serious infections occurred in single patients and resolved without clinical sequelae

after standard medical management. Certain death cases occurred in all groups, and none were considered treatment-related. The treatment discontinuation rate due to AEs was low and comparable between groups (Figure 7G, 2.52% vs. 3.49%, OR=0.72, vs. placebo;

Study or Subgroup	Experime Events		Control Events T		Weight	Odds Ratio M-H, Fixed, 95% CI	Odds Ratio M-H. Fixed, 95% Cl
1.3.1 Deucravacitinil			LVCIIIO I	otui	Weight	WHITE TREAT 0070 OF	
Armstrong,AW.2023	118	332	7	166	6.9%	12.52 [5.69, 27.59]	
NCT04167462	56	146	1	74	0.9%		
Strober, B.2023	138	511		255	7.8%	13.11 [6.03, 28.48]	
Subtotal (95% CI)		989		495	15.6%	14.79 [8.70, 25.15]	•
Total events	312		15				
Heterogeneity: Chi ² = Test for overall effect:		•					
	h 40						
1.3.2 Deucravacitini			4	45	0.00/	00 44 54 00 004 001	
Papp, K. 2018 Subtotal (95% CI)	19	44 44	1	45 45		33.44 [4.22, 264.99] 33.44 [4.22, 264.99]	
Total events	19		1	45	0.0 /0	55.44 [4.22, 204.99]	
Heterogeneity: Not ap			1				
Test for overall effect:	: Z = 3.32 (P	= 0.000	9)				
1.3.3 Deucravacitinil	h vs Anrom	ilast					
Armstrong,AW.2023	118	332	33	168	32.4%	2.26 [1.45, 3.51]	
Strober, B.2023	138	552 511		254	52.4 <i>%</i>	1.67 [1.15, 2.43]	- -
Subtotal (95% CI)	100	843		422	83.7%	1.90 [1.43, 2.43]	
Total events	256		79		/3		
Heterogeneity: Chi ² =		(P = 0.3)					
Test for overall effect:		•					
Total (95% CI)		1876	9	962 ·	100.0%	4.12 [3.26, 5.20]	•
Total events	587		95				
Heterogeneity: Chi ² =		5 (P < 0.		= 91%			
Test for overall effect:		•					0.01 0.1 1 10 10
Test for subaroup diff	(,	< 0.00	0001). I²	= 96.0%	Favours [experimental] Favours [control]
	Experim	ontal	Control			Odds Ratio	Odds Ratio
Study or Subgroup	•				Weight		
1.4.1 Deucravacitini			Evento 1	otai	weight	<u> </u>	
Armstrong,AW.2023	52	511	3	255	14.6%	9.52 [2.94, 30.78]	
NCT04167462	6	144	0	74	2.6%	6.99 [0.39, 125.85]	
Strober, B.2023	47	332		166		27.21 [3.72, 199.05]	
Subtotal (95% CI)		987		495	21.8%	12.99 [5.04, 33.51]	
Total events	105		4				
Heterogeneity: Chi ² =	· 0.98, df = 2	(P = 0.6	51); I² = 0%				
Test for overall effect	.: Z = 5.31 (P	< 0.000	01)				
	ih 12ma va	olacebo					
1.4.2 Deucravacitini							
1.4.2 Deucravacitini Papp K 2018	• •	44	Ω	45	1 5%	31 24 [1 78 548 96]	
Papp, K. 2018	11 121119 115	44 44	0	45 45		31.24 [1.78, 548.96] 31.24 [1.78, 548.96]	
Papp, K. 2018 Subtotal (95% CI)	11					31.24 [1.78, 548.96] 31.24 [1.78, 548.96]	
Papp, K. 2018	11 11		0 0				
Papp, K. 2018 Subtotal (95% CI) Total events	11 11 pplicable	44					
Papp, K. 2018 Subtotal (95% CI) Total events Heterogeneity: Not ay Test for overall effect	11 11 pplicable t: Z = 2.35 (P	44 9 = 0.02)					
Papp, K. 2018 Subtotal (95% CI) Total events Heterogeneity: Not ap Test for overall effect 1.4.3 Deucravacitini	11 11 pplicable :: Z = 2.35 (P ib vs Aprem	44 9 = 0.02) iilast	0	45	1.5%	31.24 [1.78, 548.96]	
Papp, K. 2018 Subtotal (95% CI) Total events Heterogeneity: Not ap Test for overall effect 1.4.3 Deucravacitini Armstrong,AW.2023	11 11 pplicable :: Z = 2.35 (P ib vs Aprem 47	44 9 = 0.02) iilast 332	0 5	45 168	1.5% 23.1%	31.24 [1.78, 548.96] 5.38 [2.10, 13.79]	
Papp, K. 2018 Subtotal (95% CI) Total events Heterogeneity: Not a Test for overall effect 1.4.3 Deucravacitini Armstrong,AW.2023 Strober, B.2023	11 11 pplicable :: Z = 2.35 (P ib vs Aprem	44 9 = 0.02) iilast	0 5 11	45 168 254	1.5% 23.1% 53.6%	31.24 [1.78, 548.96] 5.38 [2.10, 13.79] 2.50 [1.28, 4.88]	
Papp, K. 2018 Subtotal (95% CI) Total events Heterogeneity: Not ap Test for overall effect 1.4.3 Deucravacitini Armstrong,AW.2023	11 11 pplicable :: Z = 2.35 (P ib vs Aprem 47	44 P = 0.02) iilast 332 511	0 5 11	45 168	1.5% 23.1%	31.24 [1.78, 548.96] 5.38 [2.10, 13.79]	
Papp, K. 2018 Subtotal (95% CI) Total events Heterogeneity: Not an Test for overall effect 1.4.3 Deucravacitini Armstrong,AW.2023 Strober, B.2023 Subtotal (95% CI)	11 11 pplicable :: Z = 2.35 (P ib vs Aprem 47 52 99 = 1.70, df = 1	44 P = 0.02) iilast 332 511 843 (P = 0.1	0 5 11 16 9); I² = 41%	45 168 254 422	1.5% 23.1% 53.6%	31.24 [1.78, 548.96] 5.38 [2.10, 13.79] 2.50 [1.28, 4.88]	
Papp, K. 2018 Subtotal (95% CI) Total events Heterogeneity: Not ap Test for overall effect 1.4.3 Deucravacitini Armstrong,AW.2023 Strober, B.2023 Subtotal (95% CI) Total events Heterogeneity: Chi ² = Test for overall effect	11 11 pplicable :: Z = 2.35 (P ib vs Aprem 47 52 99 = 1.70, df = 1	44 P = 0.02) iilast 332 511 843 (P = 0.1 P < 0.000	0 5 11 16 9); I ² = 41% 1)	45 168 254 422 %	1.5% 23.1% 53.6% 76.7%	31.24 [1.78, 548.96] 5.38 [2.10, 13.79] 2.50 [1.28, 4.88] 3.37 [1.96, 5.79]	
Papp, K. 2018 Subtotal (95% CI) Total events Heterogeneity: Not ay Test for overall effect 1.4.3 Deucravacitini Armstrong,AW.2023 Strober, B.2023 Subtotal (95% CI) Total events Heterogeneity: Chi ² = Test for overall effect Total (95% CI)	11 11 pplicable :: Z = 2.35 (P ib vs Aprem 47 52 99 = 1.70, df = 1 :: Z = 4.40 (P	44 P = 0.02) iilast 332 511 843 (P = 0.1	0 5 11 16 9); I ² = 419 1)	45 168 254 422 %	1.5% 23.1% 53.6%	31.24 [1.78, 548.96] 5.38 [2.10, 13.79] 2.50 [1.28, 4.88]	
Papp, K. 2018 Subtotal (95% CI) Total events Heterogeneity: Not ap Test for overall effect 1.4.3 Deucravacitini Armstrong,AW.2023 Strober, B.2023 Subtotal (95% CI) Total events Heterogeneity: Chi ² = Test for overall effect Total (95% CI) Total events	11 11 pplicable :: Z = 2.35 (P ib vs Aprem 47 52 99 = 1.70, df = 1 :: Z = 4.40 (P 215	44 2 = 0.02) iilast 332 511 843 (P = 0.1 2 < 0.000 1874	0 5 11 9); I ² = 41% 1) 20	45 168 254 422 % 962	1.5% 23.1% 53.6% 76.7%	31.24 [1.78, 548.96] 5.38 [2.10, 13.79] 2.50 [1.28, 4.88] 3.37 [1.96, 5.79]	
Papp, K. 2018 Subtotal (95% CI) Total events Heterogeneity: Not ay Test for overall effect 1.4.3 Deucravacitini Armstrong,AW.2023 Strober, B.2023 Subtotal (95% CI) Total events Heterogeneity: Chi ² = Test for overall effect Total (95% CI) Total events Heterogeneity: Chi ² =	11 11 pplicable :: Z = 2.35 (P ib vs Aprem 47 52 99 = 1.70, df = 1 :: Z = 4.40 (P 215 = 10.55, df =	44 2 = 0.02) iilast 332 511 843 (P = 0.1 2 < 0.000 1874 5 (P = 0.	0 5 11 9); I ² = 41% 1) 20 .06); I ² = 53	45 168 254 422 % 962	1.5% 23.1% 53.6% 76.7%	31.24 [1.78, 548.96] 5.38 [2.10, 13.79] 2.50 [1.28, 4.88] 3.37 [1.96, 5.79]	
Papp, K. 2018 Subtotal (95% CI) Total events Heterogeneity: Not ap Test for overall effect 1.4.3 Deucravacitini Armstrong,AW.2023 Strober, B.2023 Subtotal (95% CI) Total events Heterogeneity: Chi ² = Test for overall effect Total (95% CI) Total events	11 11 pplicable :: Z = 2.35 (P ib vs Aprem 47 52 99 = 1.70, df = 1 :: Z = 4.40 (P 215 = 10.55, df = :: Z = 7.66 (P	44 2 = 0.02) iilast 332 511 843 (P = 0.1 2 < 0.000 1874 5 (P = 0. 2 < 0.000	0 5 11 9); I ² = 419 1) 20 .06); I ² = 53 01)	45 168 254 422 % 962 3%	1.5% 23.1% 53.6% 76.7% 100.0%	31.24 [1.78, 548.96] 5.38 [2.10, 13.79] 2.50 [1.28, 4.88] 3.37 [1.96, 5.79] 5.88 [3.74, 9.26]	0.01 0.1 1 10 10 Favours [experimental] Favours [control]
Papp, K. 2018 Subtotal (95% CI) Total events Heterogeneity: Not ap Test for overall effect 1.4.3 Deucravacitini Armstrong,AW.2023 Strober, B.2023 Subtotal (95% CI) Total events Heterogeneity: Chi ² = Test for overall effect Total (95% CI) Total events Heterogeneity: Chi ² = Test for overall effect	11 11 pplicable :: Z = 2.35 (P ib vs Aprem 47 52 99 = 1.70, df = 1 :: Z = 4.40 (P 215 = 10.55, df = :: Z = 7.66 (P	44 2 = 0.02) iilast 332 511 843 (P = 0.1 2 < 0.000 1874 5 (P = 0. 2 < 0.000	0 5 11 9); I ² = 419 1) 20 .06); I ² = 53 01)	45 168 254 422 % 962 3%	1.5% 23.1% 53.6% 76.7% 100.0%	31.24 [1.78, 548.96] 5.38 [2.10, 13.79] 2.50 [1.28, 4.88] 3.37 [1.96, 5.79] 5.88 [3.74, 9.26]	

2.37% vs. 5.21%, OR = 0.44, vs. apremilast). Moreover, all studies detected no meaningful changes in laboratory parameters associated with JAK 1/2/3 inhibitors like hematological parameters, lipid levels, and chemistry parameters during treatment, implying the potential safety of deucravacitinib.

4. Conclusion

In this research, deucravacitinib demonstrated its therapeutic benefit for the treatment of moderate to severe plaque psoriasis in multiple key endpoints, including PASI 75, sPGA 0/1, PASI 90, PASI 100,

Study or Subarrow	Experime		Contr		Moint	Odds Ratio M-H, Fixed, 95% CI	Odds	
Study or Subgroup 1.5.1 Deucravacitini			Events	TOTAL	weight	<u>wi-n, rixea, 95% Cl</u>	I IVI-FI, FIXE	d, 95% Cl
Armstrong,AW.2023	147	209	21	121	13.9%	11.29 [6.47, 19.69]		
NCT04167462	66	105	5	51	4.4%			
Strober, B.2023	182	305	30	173	27.3%			
Subtotal (95% CI)		619		345	45.6%	9.17 [6.59, 12.77]		•
Total events	395		56	4.07				
Heterogeneity: Chi ² = Test for overall effect		•		1%				
1.5.3 Deucravacitini	b vs Aprem	ilast						
Armstrong,AW.2023	43	110	21	121	21.5%	3.06 [1.67, 5.61]		
Strober, B.2023	61	166	30	173	32.8%	2.77 [1.67, 4.59]		
Subtotal (95% CI)		276		294	54.4%	2.88 [1.96, 4.25]		-
Total events	104		51					
Heterogeneity: Chi ² = Test for overall effect				%				
Total (95% CI)		895		639	100.0%	5.75 [4.50, 7.36]		◆
Total events	499		107			-		
Heterogeneity: Chi ² =	22.44, df =	4 (P = 0	.0002); I²	= 82%	D		0.01 0.1 1	10 100
Test for overall effect Test for subaroup diff	```		,	(P < 0	.00001).	² = 94.9%	Favours [experimental]	
	Experime	ntal	Contro	ol		Odds Ratio	Odds	Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixe	d, 95% Cl
1.6.1 Deucravacitinil	o 6mg vs pla	acebo						
Armstrong,AW.2023	132	322	17	160	11.1%	5.84 [3.37, 10.13]		
NCT04167462	66	105	5	51	2.1%	15.57 [5.70, 42.50]		
Strober, B.2023	186	495	24	246	16.6%	5.57 [3.52, 8.81]		•
Subtotal (95% CI) Total events	384	922	46	457	29.9%	6.37 [4.57, 8.87]		•
Heterogeneity: Chi ² = Test for overall effect:	3.47, df = 2	·	8); l² = 42	2%				
1.6.2 Deucravacitinil	o 12mg vs p	lacebo						
Papp, K. 2018	28	44	2	45	0.6%	37.63 [8.03, 176.40]		
Subtotal (95% CI)		44		45		37.63 [8.03, 176.40]		
Total events	28		2					
Heterogeneity: Not ap Test for overall effect:	•	< 0.000	01)					
1.6.3 Deucravacitinil	o vs Apremi	last						
Armstrong,AW.2023	132	322	46	161	30.1%	1.74 [1.16, 2.61]		
Strober, B.2023	186	495	57	247	39.5%	2.01 [1.42, 2.84]		
Subtotal (95% CI)		817		408	69.5%	1.89 [1.45, 2.46]		▼
Total events	318	(D	103	.,				
Heterogeneity: Chi ² = Test for overall effect:				//o				
Total (95% CI)		1783		910	100.0%	3.44 [2.82, 4.19]		•
Total events	730		151					
Heterogeneity: Chi ² =				² = 89%	6		0.01 0.1 1	10 100
Test for overall effect:	,		,	′P < 0.(00001). I²		Favours [experimental]	
Test for subaroup diff								

and DLQI 0/1 at week 16. Moreover, a durable response was seen in the two 52-week studies. Safety assessment showed that deucravacitinib was generally well tolerated, and the incidence of AEs, SAEs, and AE-related treatment discontinuation was low and balanced across groups, consistent with results observed in a previous study in healthy volunteers (20). AEs caused by the inhibition of the JAK1/2/3 signaling pathway (hematological toxicity, etc.) were rarely seen in deucravacitinib-treated patients. Clinically meaningful changes in laboratory parameters commonly observed with inhibitors of JAK 1/2/3 are not observed with deucravacitinib treatment. Extensive follow-up data collection from

POETY PSO trials showed persistent efficacy and consistent safety profiles of deucravacitinib for up to 2 years (21). Deucravacitinib has the potential to be used as the first-line oral therapy for plaque psoriasis.

5. Discussion

IL-23 and type I IFN has been demonstrated to play a crucial role in the pathogenesis of psoriasis. As they both rely on a heterodimer of JAK2 and TYK2 for signal transduction, JAK2 and

	Experimental (Events Total Ev	Control		Odds Ratio	Odds Ratio	Experimental Control Odds Ratio Odds Ratio
1.18.1 Deucravaciti	ib 6mg vs placebo				M-H. Fixed. 95% Cl	Study or Subgroup Events Total Events Total Weight M-H. Fixed. 95% Cl M-H. Fixed. 95% Cl 1.21.1 Deucravacitinib 6mg vs placebo
Armstrong,AW.2023 Mease, PJ. 2022	21 332 4 70	14 168 1 5 66	4.6%	0.74 [0.37, 1.50] 0.74 [0.19, 2.88]		Armstrong,AW.2023 21 332 6 166 15.5% 1.80 [0.71, 4.55] Mease, PJ. 2022 4 70 0 66 1.0% 9.00 [0.48, 170.49]
NCT04167462 Strober, B.2023	10 146 55 511	4 74 23 254 2	4.7% 26.0%	1.29 [0.39, 4.25] 1.21 [0.73, 2.02]		NCT04167462 26 146 4 74 9.0% 3.79 [1.27, 11.31] Strober, B.2023 25 511 11 255 28.9% 1.14 [0.55, 2.36]
Subtotal (95% CI) Total events	1059 90	562 5 46	51.8%	1.03 [0.71, 1.49]	•	Subtotal (95% CI) 1059 561 54.4% 1.91 [1.17, 3.12] Total events 76 21
Heterogeneity: Chi ² = Test for overall effect	1.58, df = 3 (P = 0.66);	I ² = 0%				Heterogeneity: Chi ² = 4.53, df = 3 (P = 0.21); l ² = 34% Test for overall effect: Z = 2.60 (P = 0.009)
	ib 12mg vs placebo					1.21.2 Deucravacitinib 12mg vs placebo
Mease, PJ. 2022	12 67		3.9% 1.8%	2.66 [0.88, 8.04]		Mease, PJ. 2022 1 67 0 66 1.0% 3.00 [0.12, 74.98] Subtotal (95% Cl) 67 66 1.0% 3.00 [0.12, 74.98]
Papp, K. 2018 Subtotal (95% CI)	111	111		1.02 [0.14, 7.61] 2.15 [0.83, 5.57]	-	Total events 1 0 Heterogeneity: Not applicable
Total events Heterogeneity: Chi ² =	14 0.67, df = 1 (P = 0.41);	7 I ² = 0%				Test for overall effect: Z = 0.67 (P = 0.50)
Test for overall effect						1.21.3 Deucravacitinib vs Apremilast Armstrong,AW.2023 21 332 3 168 7.7% 3.71 [1.09, 12.63]
1.18.3 Deucravacitie Armstrong, AW.2023	21 332	14 168 1		0.74 [0.37, 1.50]		Armstrong,AW 2023 21 332 3 168 7.7% 3.71 [1.09, 12.63] Strober, B.2023 25 511 14 254 36.8% 0.88 [0.45, 1.73] Subbtal (9% Cl) 843 422 44.5% 1.37 (10.78, 2.42]
Strober, B.2023 Subtotal (95% CI)	55 511 843	23 254 2 422 4		1.21 [0.73, 2.02] 1.03 [0.68, 1.55]	*	Total events 46 17
Total events Heterogeneity: Chi ²	76 1.22, df = 1 (P = 0.27);	37 I² = 18%				Heterogeneity: Chi ^a = 4.20, df = 1 (P = 0.04); l ^a = 76% Test for overall effect: Z = 1.09 (P = 0.27)
Test for overall effect	Z = 0.14 (P = 0.89)					Total (95% Cl) 1969 1049 100.0% 1.68 [1.17, 2.43]
Total (95% CI) Total events	2013 180	1095 10 90	0.0%	1.09 [0.84, 1.42]	•	Total events 123 38 Heterogeneity: Chi ² = 9.77, df = 6 (P = 0.13); P = 39% 0.01 0.1 1 10
Heterogeneity: Chi ² = Test for overall effect	5.51, df = 7 (P = 0.60); Z = 0.65 (P = 0.52)	I ² = 0%		0.01		Test for overall effect: Z = 2.78 (P = 0.005) 0.01 0.1 1 10 Test for subornun differences: ChiP = 0.88 df = 2 /P = 0.641 P = 0% Favours [experimental] Favours [control]
	erences: Chi ² = 2.12. df	= 2 (P = 0.35)	l² = 5.7%	F	avours [experimental] Favours [control]	
Study or Subarcon	Experimental Events Total	Control Events Total	Waiaht	Odds Ratio M-H. Fixed. 95% Cl	Odds Ratio M-H. Fixed, 95% Cl	Experimental Control Odds Ratio Odds Ratio Study or Subgroup Events Total Events Total Weight M-H, Fixed, 95% Cl M-H, Fixed, 95% Cl
1.25.1 Deucravacit	inib 6mg vs placebo					1.24.1 Deucravacitinib 6mg vs placebo
Armstrong,AW.2023 Strober, B.2023	7 511	4 166 3 255	6.0%	0.87 [0.25, 3.02] 1.17 [0.30, 4.55]		Mease, PJ. 2022 5 70 3 66 3.2% 1.62 [0.37, 7.04]
Subtotal (95% CI) Total events	843 14	421 7	13.9%	1.00 [0.40, 2.50]		Strober, B.2023 22 511 14 255 20.0% 0.77 [0.39, 1.54] Subtotal (95% Cl) 913 487 30.4% 1.06 [0.63, 1.80]
Heterogeneity: Chi ² Test for overall effe	= 0.10, df = 1 (P = 0.76 ct: Z = 0.00 (P = 1.00)	.); I ² = 0%				Total events 43 22 Heterogeneity: Chi ² = 1.80, df = 2 (P = 0.41); I ² = 0%
	inib 12mg vs placebo					Test for overall effect: Z = 0.23 (P = 0.82)
Papp, K. 2018 Subtotal (95% CI)	2 44 44	2 45 45		1.02 [0.14, 7.61] 1.02 [0.14, 7.61]		1.24.2 Deucravacitinib 12mg vs placebo Mease, PJ. 2022 2 67 3 66 3.3% 0.65 [0.10, 4.00]
Total events	2	2	±			Papp, K. 2018 2 44 2 45 2.1% 1.02 [0.14, 7.61] Subtotal (95% CI) 111 111 5.4% 0.79 [0.21, 3.04]
Heterogeneity: Not Test for overall effe	applicable st: Z = 0.02 (P = 0.98)					Total events 4 5 Heterogeneity: Chi ² = 0.11, df = 1 (P = 0.74); I ² = 0%
	inib vs Apremilast					Test for overall effect: Z = 0.34 (P = 0.74)
Armstrong,AW.202 Strober, B.2023	7 511	19 168 23 254	45.9%	0.14 [0.06, 0.33]		1.24.3 Deucravacitinib vs Apremilast Armstrong,AW.2023 16 332 17 168 24.1% 0.45 [0.22, 0.91]
Subtotal (95% CI) Total events	843 14	422	83.3%	0.15 [0.08, 0.28]	◆	Strober, B.2023 22 511 28 254 40.1% 0.36 [0.20, 0.65] Subtotal (95% CI) 843 422 64.2% 0.40 [0.25, 0.62]
Heterogeneity: Chi ²	= 0.09, df = 1 (P = 0.76 ct: Z = 5.97 (P < 0.0000	i); l ² = 0%				Total events 38 45 Heterogeneity: Chi ² = 0.21, df = 1 (P = 0.65); l ² = 0%
Total (95% CI)	1730		100.0%	0.30 [0.19, 0.47]	•	Test for overall effect: Z = 4.05 (P < 0.0001)
Total events	30	51	100.078	0.50 [0.13, 0.47]	· · · · · · · · · · · · · · · · · · ·	Total (95% Cl) 1867 1020 100.0% 0.62 [0.45, 0.86] Total events 85 72
Test for overall effe	= 12.75, df = 4 (P = 0.0 ct: Z = 5.24 (P < 0.0000	(1)			0.01 0.1 1 10 Favours [experimental] Favours [control]	100 Heterogeneity: Chi ² = 9.76, df = 6 (P = 0.14); l ² = 39% 0.01 0.1 1 10
Test for subaroun d	fferences: Chi ² = 12 67	df = 2 (P = 0	002) 12 =	84.2%		Test for suboroun differences: Chi ² = 8.01. df = 2 (P = 0.02). l ² = 75.0%
Study or Subgrou	Experimental p Events Total	Control Events Total	Weight	Odds Ratio M-H. Fixed. 95% C	Odds Ratio M-H, Fixed, 95% Cl	
1.23.1 Deucravac	tinib 6mg vs placebo					1.12.1 Deucravacitinib 6mg vs placebo
Armstrong,AW.202 Mease, PJ. 2022	5 70	5 166 3 66	3.0%	1.62 [0.37, 7.04]		Mease, PJ. 2022 0 70 1 66 5.5% 0.31 [0.01, 7.74]
NCT04167462 Strober, B.2023	8 146 22 511	4 74 14 255	19.0%	0.77 [0.39, 1.54]	- <u>+</u>	NCT04167462 4 146 1 74 4.6% 2.06 (0.23, 18.73) Strober, B.2023 8 511 3 255 14.1% 1.34 (0.35, 5.08)
Subtotal (95% CI) Total events	1059 51	561 26	34.1%	1.06 [0.65, 1.71]	₹	Subtotal (95% Cl) 1059 561 66.1% 0.69 [0.35, 1.38] Total events 19 14
Heterogeneity: Chi Test for overall effe	t = 1.80, df = 3 (P = 0.6 ct: Z = 0.22 (P = 0.82)	2); I ² = 0%				Heterogeneity: $Chi^2 = 3.52$, $df = 3$ (P = 0.32); $I^2 = 15\%$ Test for overall effect: Z = 1.04 (P = 0.30)
1.23.2 Deucravac	tinib 12mg vs placebo	,				1.12.2 Deucravacitinib 12mg vs placebo
Mease, PJ. 2022 Papp, K. 2018	1 67 2 44	3 66 2 45		0.32 [0.03, 3.14]		Mease, PJ. 2022 0 67 1 66 5.4% 0.32 [0.01, 8.08] Papp, K. 2018 0 44 1 45 5.2% 0.33 [0.01, 8.41]
Subtotal (95% CI) Total events	111	111	5.2%		-	Subtotal (95% CI) 111 111 10.6% 0.33 (0.03, 3.21) Total events 0 2
Heterogeneity: Chi	t = 0.57, df = 1 (P = 0.4 ct: Z = 0.71 (P = 0.48)	5); l ² = 0%				Heterogeneity: Chi ² = 0.00, df = 1 (P = 0.99); l ² = 0% Test for overall effect: Z = 0.96 (P = 0.34)
						1.12.3 Deucravacitinib vs Apremilast
Armstrong,AW.202		17 168				Armstrong,AW 2023 7 332 4 168 18.6% 0.88 [0.25, 3.06] Strober, B.2023 8 511 1 254 4.7% 4.02 [0.50, 32.35]
Strober, B.2023 Subtotal (95% CI)	22 511 843		38.0% 60.8%		•	Subtotal (95% Cl) 843 422 23.3% 1.52 [0.55, 4.21] Total events 15 5
Total events Heterogeneity: Chi	38 = 0.21, df = 1 (P = 0.6	45 5); I ² = 0%				Heterogeneity: Chi ² = 1.57, df = 1 (P = 0.21); l ² = 36% Test for overall effect: $Z = 0.80$ (P = 0.42)
Test for overall effe	ct: Z = 4.05 (P < 0.000	1)				Total (95% Cl) 2013 1094 100.0% 0.85 [0.49, 1.45]
Total (95% CI) Total events	2013 92	1094 76	100.0%	0.63 [0.46, 0.86]	•	Total events 34 21 Heterogeneity: Chi ² = 6.76, df = 7 (P = 0.45); P = 0% 0.01 0.1 1 10
Heterogeneity: Chi	t = 10.71, df = 7 (P = 0. ct; Z = 2.88 (P = 0.004	15); I ² = 35%			0.01 0.1 1 10	Test for overall effect: Z = 0.61 (P = 0.54) 0.01 1 10 100 Test for suboroun differences: Chi ² = 2 24. df = 2 (P = 0.33) I ² = 10.8%. Favours [control] Favours [control]
	ct: Z = 2.88 (P = 0.004 lifferences: Chi ² = 8.50		01) I² = 7	6.5%	Favours [experimental] Favours [control]	
Study or Out-		Control	Maint	Odds Ratio	Odds Ratio	
1.15.1 Deucravacit	Events Total I				M-H. Fixed. 95% Cl	
Armstrong,AW.2023 Mease, PJ. 2022	3 70	1 66	17.2% 1.8%	0.42 [0.14, 1.26] 2.91 [0.30, 28.70]		
Strober, B.2023 Subtotal (95% CI)	14 511 913	487	21.9% 40.9%	0.77 [0.33, 1.80] 0.72 [0.38, 1.35]	+	
Total events Heterogeneity: Chi ²	23 = 2.38, df = 2 (P = 0.30	17); I² = 16%				
Test for overall effe	t: Z = 1.02 (P = 0.31)					
1.15.2 Deucravacit Mease, PJ, 2022	inib 12mg vs placebo 4 67	1 66	1.8%	4.13 [0.45, 37.94]		
Papp, K. 2018 Subtotal (95% CI)	1 44 111	2 45 111	3.6% 5.4%	0.50 [0.04, 5.72]		
Total events	5 = 1.58, df = 1 (P = 0.21	3				
	= 1.58, df = 1 (P = 0.21 d: Z = 0.71 (P = 0.48)	/, r = 37%				
1.15.3 Deucravacit						
Armstrong,AW.2023 Strober, B.2023	14 511	10 168 12 254	29.2%	0.29 [0.10, 0.81] 0.57 [0.26, 1.25]		
Subtotal (95% CI)	843 20	422 22	53.7%	0.44 [0.24, 0.82]	-	
Total events); I ² = 3%				
Heterogeneity: Chi ²	t: Z = 2.59 (P = 0.009)					
Heterogeneity: Chi ² Test for overall effe	t: Z = 2.59 (P = 0.009) 1867		100 0%	0.62 [0.41 0.95]	•	
Heterogeneity: Chi ² Test for overall effe Total (95% CI) Total events	t: Z = 2.59 (P = 0.009)	1020 42	100.0%	0.62 [0.41, 0.95]	• 0.01 0.1 1 10	100

The incidence of nasopharyngitis (A), upper respiratory tract infection (B), nausea (C), diarrhea (D), headache (E), SAEs (F), AE-related discontinuations (G) in the experimental and control group.

TYK2 are potential therapeutic targets for treating psoriasis (22, 23). The pan-JAK inhibitor tofacitinib could efficiently inhibit the signal transduction of JAK 1/2/3 and TYK2 and showed superior efficacy in treating psoriasis. However, as the JAKs play an essential role in many immune responses, the low selectivity of tofacitinib toward JAK2 and TYK2 results in serious side effects, and its clinical use was strictly limited by the FDA. Developing selective TYK2 inhibitors with an acceptable safety profile was an attractive strategy for the long-term treatment of moderate to severe psoriasis (24).

Deucravacitinib is a first-in-class, highly selective oral TYK2 inhibitor with a unique mechanism of action. By binding to the residual ATP-binding site of the TYK2 pseudokinase domain rather than to the highly conserved ATP-binding sites in the catalytic domain, deucravacitinib specifically inhibits TYK2 via an allosteric mechanism, granting it significantly improved selectivity over JAK 1/2/3 and a low risk of off-target effects (25-27). TYK2 inhibition by deucravacitinib blocked both the innate (type I IFN-mediated) and adaptive (IL-23-mediated) pathways involved in psoriasis pathophysiology and resulted in optimal clinical outcomes (27). In a pooled analysis of clinical trials comparing the efficacy and safety of JAK inhibitors, deucravacitinib was superior to other approved pan-JAK inhibitors for PASI75 and PGA responses with a favorable safety profile (6). In some studies, deucravacitinib elicited efficacy for the treatment of plaque psoriasis as early as week 4, with continuous efficacy trends observed from week 2 to week 12, and greatly improved the patient's quality of life (28, 29). The approval of deucravacitinib led to an increased interest in developing selective TYK2 inhibitors and shed light on the search for an effective, safer, cheaper, and more convenient treatment of psoriasis (30).

The approval of deucravacitinib has expanded the options available to physicians treating vulnerable patients with plaque psoriasis, particularly the elderly who are often undertreated due to the presence of multiple comorbidities or the occurrence of AEs and SAEs resulting from previous treatments. A clinical trial is also ongoing to evaluate the effectiveness and safety of deucravacitinib in adolescents with plaque psoriasis (aged 12 to 18 years) (NCT04772079). The unique mechanism of selective TYK2 inhibition endows deucravacitinib with a superior safety profile compared to other approved JAK1/2/3 inhibitors and expands the scope of personalized medicine in plaque psoriasis, a holistic approach to psoriasis patients with co-morbidities is to be expected in the near future (31, 32).

5.1. Strengths and limitations

Though with encouraging outcomes, there are some limitations in this study. The first is the relatively small sample size of patients included, which may reduce the ability to detect minor potential statistically significant differences in clinical outcomes, AEs, and SAEs. Extensive retrospective studies are required to validate the efficacy and

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safety of deucravacitinib in real-world settings, especially in patients who are typically excluded from clinical trials for not meeting the strict inclusion criteria (7, 8). Moreover, five RCTs were included in the metaanalysis and a risk of publication bias may exist. The third is the long-term safety of deucravacitinib. Though current data showed consistent safety profiles of deucravacitinib for up to 2 years, information regarding the time until relapse after drug withdrawal was currently unavailable. Considering the essential role that the type I IFN pathway plays in host defense against viral and other infections, it's necessary to further evaluate the maintenance of clinical response after drug withdrawal and the long-term safety of deucravacitinib (33).

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding authors.

Author contributions

JQ: Data curation, Investigation, Writing – review & editing. JL: Writing – original draft. WL: Investigation, Writing – review & editing. FL: Conceptualization, Methodology, Project administration, Writing – review & editing. NS: Conceptualization, Project administration, Resources, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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