Αναστολείς κινάσης τυροσίνης και φωσφοδιεστεράσης 4 για την ψωρίαση του τριχωτού της κεφαλής: μια μετα-ανάλυση Efficacy of tyrosine-kinase-2 and phosphodiesterase-4 inhibitors for scalp psoriasis: a systematic review and meta-analysis. Sotirios G. Tsiogkas<sup>a</sup>, Eleni K. Karamitrou<sup>b</sup>, Maria G. Grammatikopoulou<sup>a</sup>, Efterpi Zafiriou<sup>c</sup>, Dimitrios P. Bogdanos<sup>a</sup>

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Background and aims: Scalp may be affected in about stu 80% of patients with psoriasis. Achievement of ADV. satisfactory clinical response is challenging and failure Cor to adequately control the symptoms of the disease may EST significantly impact patients' quality of life. The only  $\frac{LIBE}{POF}$ Food and Drug Administration (FDA)-approved small POE molecule inhibitors for plaque psoriasis include apremilast and deucravacitinib. Ease of administration, Tot lower cost and favorable safety profile constitute these Total agents a promising alternative for the long term management of the disease. The aim of this study was to meta-analyze data from randomized controlled trials (b) (RCTs) regarding the efficacy of oral small molecule stud POET inhibitors for the management of scalp psoriasis.

Total (95% CI)

395

Total events

(C)

Methods: We included RCTs enrolling adult patients with scalp psoriasis. Studies investigating patients with plaque psoriasis with concomitant scalp involvement were included when outcomes in the scalp-involved subpopulation were reported using scoring systems. We systematically searched Medline, Scopus, Web of Science, CENTRAL databases and ClinicalTrials.gov registry for studies fulfilling the inclusion criteria from inception until 4th August 2023. Data from RCTs were synthesized. Results of pair-wise comparisons of dichotomous data were presented as risk ratios (RR) and 95% confidence intervals (CI). Random effects model meta-analyses using an inverse variance approach were executed. Results were visualized using forest plots. Heterogeneity was assessed utilizing Q and I<sup>2</sup> statistics. To determine risk of bias of included RCTs, the revised Risk of Bias (RoB) assessment tool

(0)	Apremi	last	Place	bo		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
ADVANCE	94	212	33	199	18.1%	2.67 [1.89, 3.78]	
Core	26	59	8	53	4.4%	2.92 [1.45, 5.88]	
ESTEEM 1	174	374	33	189	20.1%	2.66 [1.92, 3.70]	
ESTEEM 2	72	176	16	93	9.4%	2.38 [1.47, 3.84]	
LIBERATE	24	54	15	58	7.8%	1.72 [1.01, 2.91]	
POETYK-PSO-1	43	110	21	121	10.6%	2.25 [1.43, 3.54]	
POETYK-PSO-2	61	166	30	173	14.9%	2.12 [1.45, 3.10]	
STYLE	87	201	14	102	8.3%	3.15 [1.89, 5.26]	
UNVEIL	42	112	11	55	6.4%	1.88 [1.05, 3.35]	
Total (95% CI)		1464		1043	100.0%	2.41 [2.08, 2.79]	•
Total events	623		181				
Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 4.87, df = 8 (P = 0.77); i <sup>2</sup> = 0%							
Test for overall effect: Z = 11.70 (P < 0.00001) 0.2 0.3 1 2 5 Favours Placebo Favours Apremilast							
(b)							
Deucravacitinib		Placebo			Risk Ratio	Risk Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl
POETYK-PSO-1	147	209	21	121	38.3%	4.05 [2.72, 6.04]	
POETYK-PSO-2	182	305	30	173	53.2%	3.44 [2.45, 4.83]	-∎-
POETYK-PSO-3	66	105	5	51	8.5%	6.41 [2.75, 14.93]	

619 3.86 [3.02, 4.94] 345 100.0% 56 Heterogeneity: Tau<sup>2</sup> = 0.00; Chi<sup>2</sup> = 1.88, df = 2 (P = 0.39); l<sup>2</sup> = 0% 0.01 Test for overall effect: Z = 10.74 (P < 0.00001) Favours Placebo Favours Deucravacitinib

**Risk Ratio Risk Ratio** Deucravacitinib Apremilast Study or Subgroup Events Total Events Total Weight IV, Random, 95% Cl IV. Random, 95% CI POETYK-PSO-1 147 209 43 110 43.7% 1.80 [1.40, 2.31] POETYK-PSO-2 182 305 61 166 56.3% 1.62 [1.30, 2.02] Total (95% CI) 514 276 100.0% 1.70 [1.44, 2.00] Total events 329 104 Heterogeneity: Tau<sup>2</sup> = 0.00; Chi<sup>2</sup> = 0.37, df = 1 (P = 0.55); l<sup>2</sup> = 0% h 2 0.5 Test for overall effect: Z = 6.30 (P < 0.00001 Favours Apremilast Favours Deucravacitinib

Results: In total, our search retrieved 495 reports. <sup>–</sup>Duplicates were deleted and 353 reports were screened, of which 227 were excluded. Finally, 30 entries corresponding to 10 RCTs were included in the systematic review and meta-analyses. Six of the 10 included studies were rated as of low risk of overall bias, 3 as exhibiting some concerns and 1 as of high risk of overall bias.

Apremilast (30 mg twice daily, RR 2.41, 95% CI 2.08 to 2.79) and deucravacitinib (6 mg daily, RR 3.86, 95% CI 3.02 to 4.94) are more effective than placebo in clearing or almost clearing the psoriatic scalp (achieving a Scalp Physician's Global Assessment [ScPGA] of 0 or 1) at 16 weeks post treatment initiation.

Deucravacitinib is more effective than apremilast in clearing or almost clearing the psoriatic scalp (RR 1.70, 95% CI 1.44 to 2.00).

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**Conclusions:** Apremilast and deucravacitinib are effective and well tolerated oral agents for the management of scalp psoriasis. The efficacy of apremilast is well established over the last decade. Deucravacitinib may be more efficient in clearing the scalp, but research is warranted.

Figure 1. Forest plots depicting the results of the meta-analyses. (a) Apremilast is more effective than placebo in inducing cleared or almost cleared skin at 16 weeks. (b) Deucravacitinib is more effective than placebo in inducing cleared or almost cleared skin at 16 weeks. (c) Deucravacitinib is more effective than apremilast in inducing cleared or almost cleared skin at 16 weeks.



