Deucravacitinib, an oral selective tyrosine kinase 2 (TYK2) inhibitor, in patients with moderate to severe scalp psoriasis: efficacy and safety results of a phase 3b/4, multicenter, randomized, double-blinded, placebo-controlled trial (PSORIATYK SCALP)

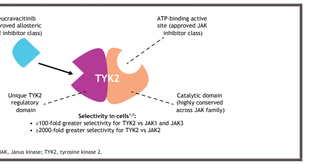
Kristina Callis Duffin,[1] Christopher E. M. Griffiths,[2] Matthias Hoffmann,[3] Andrew Blauvelt,[4] Eugene Balagula,[5] Andrew Napoli,[5] Ying-Ming Jou,[5] Rachel Dyme,[5] Virginia Hala,[5] Andreas Pinter,[6] Mark Lebwohl[7]

[1]University of Utah, Salt Lake City, UT, USA; [2]Dermatology Centre, University of Manchester, Manchester, and King's College Hospital and King's College London, London, UK; [3]Private Practice, Witten, Germany; [4]Blauvelt Consulting, Portland, OR, USA; [5]Bristol Myers Squibb, Princeton, NJ, USA; [6]University Hospital of the Goethe University, Frankfurt am Main, Germany; [7]Icahn School of Medicine at Mount Sinai, New York, NY, USA

Synopsis

- Tyrosine kinase 2 (TYK2) is an intracellular enzyme that mediates signaling of select inflammatory cytokines (eg, interleukin [IL]-23, IL-12, Type I interferons [IFNs])[1]
  - IL-23 and Type I IFNs are involved in psoriasis pathogenesis[1]
- Deucravacitinib, an oral, selective, allosteric TYK2 inhibitor, is approved in the US, EU, and other countries for the treatment of adults with moderate to severe plaque psoriasis who are candidates for systemic therapy[2-6]
- Deucravacitinib uniquely binds to the TYK2 regulatory domain rather than to the catalytic domain where Janus kinase (JAK) 1,2,3 inhibitors bind[1,7] (**Figure 1**), driving its selectivity for TYK2 and representing the first in a new class of oral drugs
- Deucravacitinib demonstrated a robust efficacy and safety profile in the global phase 3 POETYK PSO-1 (NCT03624127) and POETYK PSO-2 (NCT03611751) trials in patients with moderate to severe plaque psoriasis[8,9]

Figure 1. Mechanism of action of deucravacitinib



ATP, adenosine 5'-triphosphate; JAK, Janus kinase; TYK2, tyrosine kinase 2.

- Scalp psoriasis, which may occur in up to 80% of patients with psoriasis and is associated with itching, flaking, pain, and bleeding, disproportionately reduces quality of life and is challenging to treat with topical agents[10-16]
- In POETYK PSO-1 and PSO-2, deucravacitinib was superior to placebo at Week 16 in the subpopulation of patients with moderate to severe scalp psoriasis (scalp-specific Physician Global Assessment [ss-PGA] score ≥3 at baseline)[16]
  - In POETYK PSO-1, ss-PGA score of 0 (clear) or 1 (almost clear) (ss-PGA 0/1) and ≥90% improvement from baseline in Psoriasis Scalp Severity Index (PSSI 90) response rates were maintained through Week 52 in patients continuously treated with deucravacitinib[16]

Objective

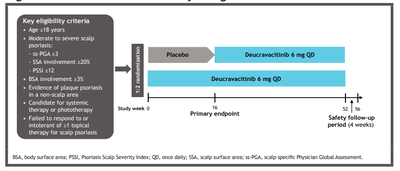
- To evaluate the efficacy and safety of deucravacitinib in patients with moderate to severe scalp psoriasis, including those with more limited overall psoriasis (body surface area [BSA] involvement ≥3%)
  - Patients in this group are candidates for systemic therapy according to the American Academy of Dermatology/National Psoriasis Foundation and International Psoriasis Council guidelines[11,14]

Methods

Study design

- PSORIATYK SCALP (NCT005478499) is an ongoing phase 3b/4, multicenter, randomized, double-blinded, placebo-controlled trial designed to evaluate the efficacy and safety of deucravacitinib in patients with moderate to severe scalp psoriasis (**Figure 2**)
  - Patients were randomized 1:2 to oral placebo or deucravacitinib 6 mg once daily (QD)
  - At Week 16, all patients were switched to open-label deucravacitinib 6 mg QD through Week 52
- Stratification factors included in randomization:
  - Prior use of biologic therapy for psoriasis, psoriatic arthritis, or other inflammatory disease (yes/no)
  - Body weight (≥90 kg/<90 kg)

Figure 2. PSORIATYK SCALP study design



BSA, body surface area; PSSI, Psoriasis Scalp Severity Index; QD, once daily; SSA, scalp surface area; ss-PGA, scalp-specific Physician Global Assessment.

- PSORIATYK SCALP included patients with moderate to severe scalp psoriasis defined by more focused and objective inclusion criteria and less extensive overall body psoriasis (BSA involvement 3%-10%) compared with the phase 3 POETYK PSO-1 and PSO-2 trials

Primary endpoint

- ss-PGA 0/1 (investigator-administered assessment)

Key secondary endpoints

- PSSI 90 (investigator-administered assessment)
- Change from baseline in scalp-specific itch numeric rating scale (NRS) (patient-reported assessment)
- Static Physician Global Assessment score of 0 (clear) or 1 (almost clear) (sPGA 0/1) (investigator-administered assessment)
  - A multiplicity control procedure prespecified this hierarchical endpoint order

Exploratory endpoints

- sPGA 0/1 response rates at Week 16 by baseline BSA involvement (3%-10% vs >10%)
- Scalp-specific itch NRS response rates (≥4-point reduction) at Week 16
- ss-PGA 0/1 response rates between Weeks 0 and 16

Safety endpoints

- Treatment-emergent adverse events (TEAEs), serious AEs, laboratory parameters, and vital signs for Weeks 0 to 16

Efficacy population

- Full analysis set: all patients who were randomized to treatment
- sPGA ≥3 subpopulation: all patients who were randomized to treatment and had baseline sPGA ≥3

Statistical analysis

- Efficacy was analyzed after all randomized patients had completed their Week 16 visit or had discontinued treatment prior to Week 16
- Nonresponder imputation (NRI) was used for binary efficacy endpoints for patients who had missing endpoint data
  - The *P* values were obtained using a stratified Cochran-Mantel-Haenszel test with stratification factors of prior biologic therapy (yes/no) and body weight (≥90 kg/<90 kg) per randomization
- Modified baseline observation carried forward (mBOCF) was used to impute missing data for continuous outcomes (ie, scalp-specific itch NRS)
  - Adjusted means, 95% confidence intervals (CIs), and *P* values were based on an analysis of covariance model with treatment, randomization stratification factors (prior biologic therapy [yes/no] and body weight [≥90 kg/<90 kg]) as fixed effects and baseline value as a covariate

Results

Patient disposition

- A total of 154 patients were randomized (placebo, n = 51; deucravacitinib, n = 103) (**Table 1**)
  - 90% of patients in each group completed treatment
  - AEs and withdrawal from the trial by the patient were the most common reasons for treatment discontinuation

Table 1. Patient disposition through Week 16

Parameter	Placebo (n = 51) n (%)	Deucravacitinib (n = 103) n (%)
Received treatment	51 (100)	103 (100)
Randomized and treated	51 (100)	103 (100)
Completed treatment	46 (90.2)	93 (90.3)
Did not complete treatment	5 (9.8)	9 (8.7)
Not reported	0	1 (1.0)
Reason for not completing treatment	5 (9.8)	9 (8.7)
Adverse event	2 (3.9)	4 (3.9)
Withdrawal by patient	2 (3.9)	3 (2.9)
Lack of efficacy	0	1 (1.0)
Lost to follow-up	0	1 (1.0)
Other	1 (2.0)	0
Death	0	0
Noncompliance with protocol	0	0

Baseline patient demographics and disease characteristics

- Baseline patient demographics and disease characteristics were similar between groups (placebo: mean BSA involvement 10.0%, Psoriasis Area and Severity Index [PASI] 9.4, PSSI 32.2; deucravacitinib: mean BSA involvement 10.5%, PASI 10.2, PSSI 33.5) (**Table 2**)

Table 2. Baseline patient demographics and disease characteristics

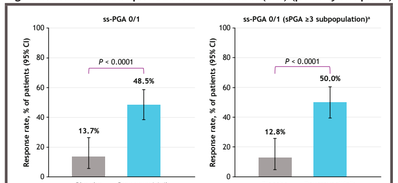
Parameter	Placebo (n = 51)	Deucravacitinib (n = 103)
Age, mean (SD), y	43.2 (13.1)	42.8 (15.7)
Weight, mean (SD), kg	88.3 (27.6)	89.3 (23.8)
Body mass index, mean (SD), kg/m^2	29.2 (7.0)	30.1 (7.1)
Female, n (%)	20 (39.2)	45 (43.7)
Race, n (%)		
White	47 (92.2)	93 (90.3)
Asian	2 (3.9)	3 (2.9)
Black or African American	2 (3.9)	5 (4.9)
Other	0	2 (1.9)
Psoriasis vulgaris duration, mean (SD), y	11.9 (9.8)	16.1 (11.4)
Scalp psoriasis duration, mean (SD), y	12.4 (9.6)	16.4 (11.7)
Prior systemic therapy, n (%)		
Yes	27 (52.9)	54 (52.4)
Prior systemic biologic	16 (31.4)	37 (35.9)
Prior systemic nonbiologic	11 (21.6)	17 (16.5)
No	24 (47.1)	49 (47.6)
ss-PGA score, n (%)		
3 (moderate)	32 (62.7)	76 (73.8)
4 (severe)	19 (37.3)	27 (26.2)
PSSI score, mean (SD)	32.2 (13.7)	33.5 (12.5)
Scalp-specific itch NRS score, mean (SD)	6.4 (1.8)	6.4 (2.3)
sPGA score, n (%)		
2 (mild)	4 (7.8)	7 (6.8)
3 (moderate)	42 (82.4)	81 (78.6)
4 (severe)	5 (9.8)	15 (14.6)
BSA involvement, mean (SD), %	10.0 (8.1)	10.5 (9.6)
PASI score, mean (SD)	9.4 (5.6)	10.2 (6.7)

BSA, body surface area; NRS, numeric rating scale; PASI, Psoriasis Area and Severity Index; PSSI, Psoriasis Scalp Severity Index; SD, standard deviation; sPGA, static Physician Global Assessment; ss-PGA, scalp-specific Physician Global Assessment.

Efficacy

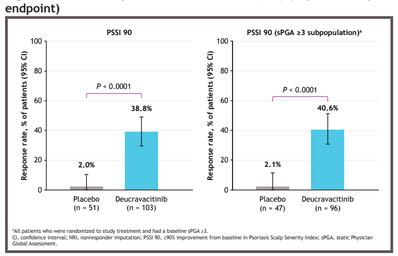
- A significantly greater proportion of deucravacitinib-treated patients achieved ss-PGA 0/1 at Week 16 compared with patients receiving placebo in both the overall population and in the subpopulation of patients with sPGA ≥3 at baseline (**Figure 3**)
- Deucravacitinib was also superior to placebo for PSSI 90 response rate (**Figure 4**) and mean change from baseline in scalp-specific itch NRS (**Figure 5**) at Week 16 in each population
- In the subpopulation of patients with sPGA ≥3 at baseline, a greater proportion achieved an overall psoriasis response of sPGA 0/1 at Week 16 with deucravacitinib vs placebo (**Figure 6**)
  - sPGA 0/1 response rates at Week 16 were significantly greater with deucravacitinib than with placebo regardless of baseline BSA involvement (3%-10% vs >10%) (**Figure 7**)
- A significantly higher proportion of deucravacitinib-treated patients in the overall population achieved a ≥4-point reduction from baseline in scalp-specific itch NRS at Week 16 compared with patients receiving placebo (**Figure 8**)
  - An improvement of ≥4 points in the scalp-specific itch NRS score is considered clinically meaningful[17]
- The superior efficacy of deucravacitinib vs placebo was evident for achievement of ss-PGA 0/1 by Week 4 in the overall population (**Figure 9**)

Figure 3. ss-PGA 0/1 response rates at Week 16 (NRI) (primary endpoint)



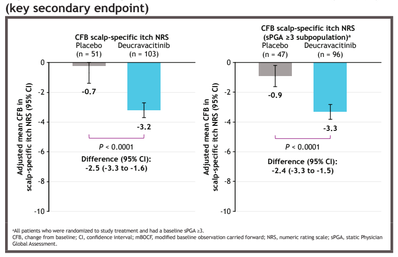
*All patients who were randomized to the study treatment and had a baseline sPGA ≥3.
CI, confidence interval; NRI, nonresponder imputation; sPGA, static Physician Global Assessment; ss-PGA, scalp-specific Physician Global Assessment.

Figure 4. PSSI 90 response rates at Week 16 (NRI) (key secondary endpoint)



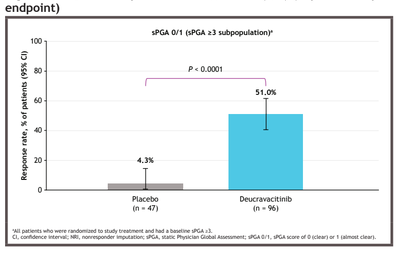
*All patients who were randomized to study treatment and had a baseline sPGA ≥3.
CI, confidence interval; NRI, nonresponder imputation; PSSI 90, ≥90% improvement from baseline in Psoriasis Scalp Severity Index; sPGA, static Physician Global Assessment.

Figure 5. CFB in scalp-specific itch NRS score at Week 16 (mBOCF) (key secondary endpoint)



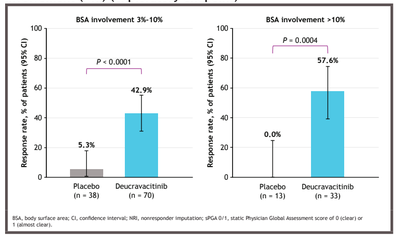
*All patients who were randomized to study treatment and had a baseline sPGA ≥3.
CFB, change from baseline; CI, confidence interval; mBOCF, modified baseline observation carried forward; NRS, numeric rating scale; sPGA, static Physician Global Assessment.

Figure 6. sPGA 0/1 response rate at Week 16 (NRI) (key secondary endpoint)



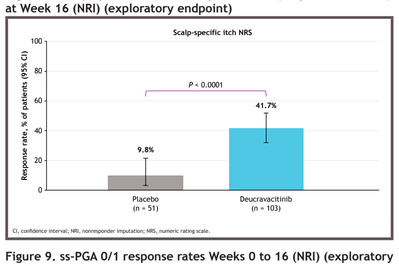
*All patients who were randomized to study treatment and had a baseline sPGA ≥3.
CI, confidence interval; NRI, nonresponder imputation; sPGA, static Physician Global Assessment; sPGA 0/1, sPGA score of 0 (clear) or 1 (almost clear).

Figure 7. sPGA 0/1 response rates at Week 16 by baseline BSA involvement (NRI) (exploratory endpoint)



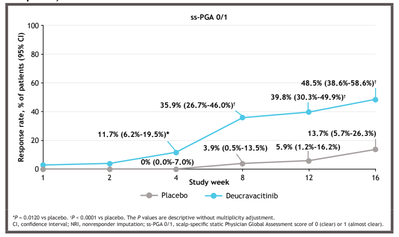
BSA, body surface area; CI, confidence interval; NRI, nonresponder imputation; sPGA 0/1, static Physician Global Assessment score of 0 (clear) or 1 (almost clear).

Figure 8. Scalp-specific itch NRS response rates (≥4-point reduction) at Week 16 (NRI) (exploratory endpoint)



CI, confidence interval; NRI, nonresponder imputation; NRS, numeric rating scale.

Figure 9. ss-PGA 0/1 response rates Weeks 0 to 16 (NRI) (exploratory endpoint)



*P = 0.0120 vs placebo. †P < 0.0001 vs placebo. The *P* values are descriptive without multiplicity adjustment.
CI, confidence interval; NRI, nonresponder imputation; ss-PGA 0/1, scalp-specific static Physician Global Assessment score of 0 (clear) or 1 (almost clear).

- **Figure 10** illustrates the improvement in moderate to severe scalp psoriasis in a deucravacitinib-treated patient from baseline to Week 16

Figure 10. Efficacy of deucravacitinib treatment in a patient with moderate to severe scalp psoriasis

Measure	Baseline (Day 1)	Week 16
ss-PGA score	4	0
PSSI score	36	0

PSSI, Psoriasis Scalp Severity Index; ss-PGA, scalp-specific Physician Global Assessment.

Safety

- TEAEs were more common in the deucravacitinib group than in the placebo group through Week 16 (**Table 3**)
  - The most common TEAEs in the deucravacitinib group (≥5%) were nasopharyngitis, upper respiratory tract infection, acne, headache, COVID-19, and acne (pustular)
    - None of the acne events were serious and only 1 patient with acne in the deucravacitinib group discontinued treatment
- Serious TEAEs and TEAEs resulting in discontinuation occurred at low incidence rates in each group
  - 2 serious TEAEs were reported (1 per group); neither event was considered treatment related or led to treatment discontinuation

Table 3. Overall safety summary, Weeks 0 to 16

TEAE category	Placebo (n = 51) n (%)	Deucravacitinib (n = 103) n (%)
Any TEAE	26 (51.0)	73 (70.9)
Serious TEAEs[a]	1 (2.0)	1 (1.0)
TEAEs leading to discontinuation	2 (3.9)	5 (4.9)
Deaths	0	0
Most common TEAEs (≥5% in the deucravacitinib group)		
Nasopharyngitis	7 (13.7)	15 (14.6)
Upper respiratory tract infection	2 (3.9)	12 (11.7)
Acne	0	10 (9.7)
Headache	2 (3.9)	8 (7.8)
COVID-19	4 (7.8)	6 (5.8)
Acne (pustular)	0	6 (5.8)

[a]Serious TEAEs: meniscus injury in the deucravacitinib group and atrial fibrillation in the placebo group. Neither event was related to treatment nor led to discontinuation. All reported AEs occurred during Weeks 0 to 16. One patient in the deucravacitinib group discontinued after Week 16 due to an AE that occurred during Weeks 0 to 16.
AE, adverse event; TEAE, treatment-emergent adverse event.

Conclusions

- In PSORIATYK SCALP, a scalp-specific trial, deucravacitinib was efficacious and well tolerated in patients with moderate to severe scalp psoriasis, including in those with less extensive overall psoriasis (BSA involvement 3%-10%; 68% of patients)
  - Patients enrolled in PSORIATYK SCALP had more severe scalp disease, based on baseline PSSI (mean, 33.5), compared with patients enrolled in the phase 3 POETYK PSO-1 and PSO-2 trials (mean, 24.6)[16]
- Deucravacitinib achieved statistical superiority vs placebo for the primary and all secondary efficacy endpoints at Week 16
  - The overall psoriasis response rate (sPGA 0/1) was consistent with results from POETYK PSO-1 and PSO-2, despite PSORIATYK SCALP including patients with more limited BSA involvement
- Safety findings were consistent with the known safety profile for deucravacitinib, with no new safety signals observed
  - No clinically meaningful mean changes from baseline in laboratory parameters were reported over 16 weeks; signature laboratory changes commonly seen with JAK1,2,3 inhibitors were not reported with deucravacitinib (data not shown)[18]
- These results support the efficacy and safety of once-daily oral deucravacitinib in patients with moderate to severe scalp psoriasis, including those with less extensive overall body psoriasis (BSA ≥3%)

References

1. Burke JR, et al. *Sci Transl Med*. 2019;11:eaaw1736. **2.** Sotyktu [package insert]. Princeton, NJ: Bristol Myers Squibb; September 2022. **3.** Sotyktu [European summary of product characteristics]. Dublin, Ireland: Bristol Myers Squibb EEIG; December 2023. **4.** Sotyktu [package insert]. Tokyo, Japan: Bristol Myers Squibb K.K.; September 2022. **5.** Sotyktu [product monograph]. Montreal, Canada: Bristol Myers Squibb Canada Co.; November 2022. **6.** Sotyktu [product information]. Mulgrave, VIC, Australia: Bristol Myers Squibb Australia Pty. Ltd.; December 2022. **7.** Wrobleski ST, et al. *J Med Chem*. 2019;62:8971-8995. **8.** Armstrong AW, et al. *J Am Acad Dermatol*. 2023;88:29-39. **9.** Strober B, et al. *J Am Acad Dermatol*. 2023;88:40-51. **10.** Kragballe K. *Curr Probl Dermatol*. 2009;38:160-171. **11.** Chan CS, et al. *J Am Acad Dermatol*. 2009;60:962-971. **12.** Rich P, et al. *J Am Acad Dermatol*. 2016;74:134-142. **13.** Papp K, et al. *J Eur Acad Dermatol Venereol*. 2007;21:1151-1160. **14.** Kragballe K, et al. *J Dermatol Treat*. 2013;24:188-192. **15.** Mason AR, et al. *Br J Dermatol*. 2013;169:519-527. **16.** Blauvelt A, et al. *J Am Acad Dermatol*. 2024;90:775-782. **17.** Wang Y, et al. *J Dermatol Treat*. 2019;30:775-783. **18.** Winthrop KL. *Nat Rev Rheumatol*. 2017;13:234-243.

Acknowledgments

- This study was sponsored by Bristol Myers Squibb
- Writing and editorial assistance was provided by Kimberly MacKenzie, PhD, of Peloton Advantage, LLC, an OPEN Health company, funded by Bristol Myers Squibb

Disclosures

KCD: Consultant (with honoraria): AbbVie, Amgen/Celgene, Boehringer Ingelheim, Bristol Myers Squibb, CorEvitas Psoriasis Registry, Janssen, Leo Pharma, Lilly, Novartis, Pfizer, and Stiefel; Speaker: Novartis; Investigator: AbbVie, Amgen/Celgene, Boehringer Ingelheim, Bristol Myers Squibb, Janssen, Lilly, Novartis, Pfizer, Regeneron, Stiefel, and UCB. **CEMG:** Honoraria and/or research grants: AbbVie, Almirall, Amgen, AnaptysBio, Boehringer Ingelheim, Bristol Myers Squibb, Evelo Biosciences, GSK, Innoagnine, Janssen, Kyowa Kirin, Leo Pharma, Lilly, Novartis, ONO Pharmaceuticals, Pfizer, Sanofi, and UCB. **MH:** Advisory boards: AbbVie, Almirall, Dermasence, Galderma, Incyte, Janssen, Leo Pharma, Leti Pharma, Novartis, Pfizer, Sanofi, and UCB; Consultant: AbbVie, Almirall, Dermasence, Galderma, Incyte, Janssen, Leo Pharma, Leti Pharma, Novartis, Pfizer, Sanofi, and UCB; Investigator: AbbVie, ALK, Almirall, Alumis, Amgen, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, Dermasence, Dermira, Forward, Galderma, Incyte, Janssen, Kiniksa, Leo Pharma, Leti Pharma, Lilly, Meda Pharma, Medac, Meiji Pharma, MSD, Nektar Therapeutics, Novartis, Pierre Fabre, Pfizer, Sanofi, Schering-Plough, Sinersud Medical Research, Stallergenes Greer, and UCB. **AB:** Speaker (with honoraria): Lilly and UCB; Scientific adviser (with honoraria): AbbVie, Abcentra, Aclaris, Affibody, Aligos, Almirall, Alumis, Amgen, AnaptysBio, Apogee, Arcutis, Arena, Aslan, Athenex, Bluefin Biomedicine, Boehringer Ingelheim, Bristol Myers Squibb, Cara Therapeutics, Cellidex, CTI BioPharma, Dermavant, Ecoffi, Escient, Evelo Biosciences, Evommune, Forte, Galderma, Highlight Pharma, Incyte, Innoventbio, Janssen, Landos, Leo Pharma, Lilly, Lipidio, Microbion, Merck, Monte Rosa Therapeutics, Nektar, Novartis, Overtone Therapeutics, Paragon, Pfizer, Q32 Bio, Rani, Rapt, Regeneron, Sanofi Genzyme, Spherix Global Insights, Sun Pharma, Takeda, TLL Pharmaceutical, TrialSpark, UCB, Union, Ventyx, Vibliome, and Xencor; Clinical study investigator (institution received clinical study funds): AbbVie, Acelyrin, Ailakos, Almirall, Alumis, Amgen, Arcutis, Athenex, Boehringer Ingelheim, Bristol Myers Squibb, Concert, Dermavant, DermBiont, Evelo Biosciences, Evommune, Galderma, Incyte, Janssen, Leo Pharma, Lilly, Merck, Novartis, Pfizer, Regeneron, Sanofi, Sun Pharma, Takeda, UCB, and Ventyx; Stock owner: Lipidio and Oruka. **EB, AN, Y-MJ, RD, and VH:** Employees and shareholders: Bristol Myers Squibb. **AP:** Advisor, paid speaker, and/or clinical trial investigator: AbbVie, Almirall-Hermal, Amgen, Biogen Idec, Biontec, Bristol Myers Squibb, Boehringer Ingelheim, Celgene, Celltrion, GSK, Eva Pharma, Galderma, Hexal, Incyte, Janssen-Cilag, Klinge Pharma, Leo Pharma, Lilly, MC2, Medac, Merck, Merck Serono, Mitsubishi, MoonLake Immunotherapeutics, Novartis, Pascoe, Pfizer, Tigercat Pharma, Regeneron, Roche, Sandoz Biopharmaceuticals, Sanofi Genzyme, Schering-Plough, UCB, and Zülig Pharma. **ML:** Research funds on behalf of Mount Sinai: AbbVie, Amgen, Arcutis, Avotres, Boehringer Ingelheim, Cara Therapeutics, Dermavant Sciences, Incyte, Janssen, Lilly, OrthoDermatologics, Regeneron, and UCB; Consultant: Almirall, Altrubio, AnaptysBio, Arcutis, Avotres, Brickell Biotech, Boehringer Ingelheim, Bristol Myers Squibb, Castle Biosciences, CorEvitas Psoriasis Registry, Dermavant, EPI Health, Evommune, Forte Biosciences, Galderma, Genentech, Incyte, Leo Pharma, Meiji Seika Pharma, Mindera Health, Pfizer, Seanergy, Strata, Trevi, and Verrica.

Scientific Content on Demand

To view a copy of this poster:

Scan the QR code via a barcode reader application

QR codes are valid for 1 year after the congress presentation date.

Presented at the 44th Annual Fall Clinical Dermatology Conference; October 24-27, 2024; Las Vegas, NV
This is an encore of the 2024 European Academy of Dermatology & Venereology Congress poster

Email: kristina.duffin@hsc.utah.edu

Copies of this poster obtained through QR (Quick Response) and/or text key codes are for personal use only and may not be reproduced without written permission from the authors.