Efficacy and safety of the oral Janus kinase 1 inhibitor povorcitinib (INCB054707) in patients with hidradenitis suppurativa in a phase 2, randomized, double-blind, dose-ranging, placebo-controlled study

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Background: Janus kinase 1 inhibition may alleviate hidradenitis suppurativa (HS)-associated inflammation and improve symptoms.

Objective: To assess efficacy and safety of povorcitinib (selective oral Janus kinase 1 inhibitor) in HS.

Methods: This placebo-controlled phase 2 study randomized patients with HS 1:1:1:1 to receive povorcitinib 15, 45, or 75 mg or placebo for 16 weeks. Primary and key secondary end points were mean change from baseline in abscess and inflammatory nodule count and percentage of patients achieving HS Clinical Response at week 16.

Results: Of 209 patients randomized (15 mg, n = 52; 45 mg, n = 52; 75 mg, n = 53; placebo, n = 52), 83.3% completed the 16-week treatment. At week 16, povorcitinib significantly reduced abscess and inflammatory nodule count from baseline (least squares mean [SE] change: 15 mg, −5.2 [0.9], P = .0277; 45 mg, −6.9 [0.9], P = .0006; 75 mg, −6.3 [0.9], P = .0021) versus placebo (−2.5 [0.9]). More povorcitinib-treated patients achieved HS Clinical Response at week 16 (15 mg, 48.1%, P = .0445; 45 mg, 44.2%, P = .0998; 75 mg, 45.3%, P = .0829) versus placebo (28.8%). A total of 60.0% and 65.4% of povorcitinib- and placebo-treated patients had adverse events.

Limitations: Baseline lesion counts were mildly imbalanced between groups.

Conclusion: Povorcitinib demonstrated efficacy in HS, with no evidence of increased incidence of adverse events among doses. (J Am Acad Dermatol 2024;90:521-9.)

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INTRODUCTION

Hidradenitis suppurativa (HS) is a chronic inflammatory condition characterized by painful skin nodules and abscesses. Draining tunnels, irreversible tissue damage, and scarring occur in severe disease stages.[1] HS has profound negative effects on quality of life (QoL)[1] that can manifest as anxiety, depression, social withdrawal, unemployment, and suicidal thoughts.[2,3] The overall estimated prevalence of HS is approximately 0.4% (95% CI, 0.26%-0.63%) but varies widely across geographic regions.[4] Demographics may also affect HS pathogenesis, although the role is not well understood. For example, Black and biracial patients in the United States have a higher HS prevalence and possibly earlier disease onset.[5-7]

Current HS medical treatments primarily consist of topical or oral antibiotics and, for moderate to severe disease, biologics.[8] Early antiinflammatory therapy is preferable to minimize risk of tissue destruction that may lead to surgical intervention.[9] Adalimumab, an anti–tumor necrosis factor alpha monoclonal antibody, was the first therapy approved by health authorities for HS.[10-12] However, many patients experience lack of initial response or loss of efficacy after a primary response with adalimumab.[10,11,13-15] There is a need for novel treatments offering robust efficacy, QoL improvements, a favorable risk-benefit profile, and convenient administration.

High proinflammatory cytokine levels contribute to HS pathogenesis by driving inflammation through multiple signaling pathways, including the Janus kinase (JAK)/signal transducer and activator of transcription pathway.[16-21] Disruption of the inflammatory cascade through JAK/signal transducer and activator of transcription inhibition may alleviate inflammation, reduce disease activity, and hinder disease progression.[22-25]

Povorcitinib (INCB054707) is an oral, small-molecule, selective JAK1 inhibitor.[26] Two proof-of-concept phase 2 studies demonstrated that povorcitinib was associated with improved outcomes and was generally well tolerated in patients with moderate to severe HS.[26] Here, we describe the efficacy and safety of 3 povorcitinib doses over 16 weeks of treatment in a larger phase 2 study of HS (NCT04476043; EudraCT Number, 2020-001981-13).

CAPSULE SUMMARY

- Hidradenitis suppurativa is a chronic and heterogeneous disease with high unmet need for novel, safe, and effective therapies.
- Povorcitinib, an oral, selective Janus kinase 1 inhibitor, reduced abscess, inflammatory nodule, and draining tunnel counts compared with placebo and was generally well tolerated across doses.

CAPSULE SUMMARY

METHODS

Patients and study design

This phase 2, multicenter, parallel-group, placebo-controlled, randomized study of povorcitinib in HS was conducted in North America and Europe. Eligible patients were 18 to 75 years old with HS for ≥3 months before screening and total abscess and inflammatory nodule (AN) count ≥5 in ≥2 distinct anatomic areas at screening and baseline. Prior HS treatment was not required except in Germany, where inadequate response or intolerance to an adequate course of antibiotics for HS was needed. Concomitant use of topical antiseptics or topical or oral antibiotics for HS was prohibited. Patients were excluded if they had >20 draining tunnels at screening or baseline; abnormal laboratory parameters at screening; inadequate response to any prior JAK inhibitor; immunomodulating biologics within 12 weeks/5 half-lives; or any other therapy that could interfere with HS course, severity, or assessment. Patients could continue analgesics (opioids or nonopioids) and medical cannabis as needed.

An interactive response technology system was used to assign patient identification numbers, track visits, randomize patients per prespecified characteristics, and mask trial-group assignments. Patients were stratified by geographic region (North America or Europe) and Hurley grade (Hurley I, II, III; Hurley III ≤25.0%) and were randomly assigned 1:1:1:1 to povorcitinib 15, 45, or 75 mg or matching placebo once daily for 16 weeks (Supplementary Fig 1, available via Mendeley at https://data.mendeley.com/datasets/hpc4rpv6j8/1). Patients, investigators, and the sponsor remained unaware of trial-group assignments throughout the placebo-controlled period, which is being followed by 2 distinct open-

Abbreviations used:

AN:	abscess and inflammatory nodule
DLQI:	Dermatology Life Quality Index
FACIT-F:	Functional Assessment of Chronic Illness Therapy—Fatigue
HiSCR:	Hidradenitis Suppurativa Clinical Response
HiSQoL:	Hidradenitis Suppurativa Quality of Life
HS:	hidradenitis suppurativa
IHS4:	International Hidradenitis Suppurativa Severity Score System
JAK:	Janus kinase
NRS:	numerical rating scale
QoL:	quality of life
SAE:	serious adverse event
TEAE:	treatment-emergent adverse event

label treatment periods that will be reported separately. This study was conducted in accordance with the Declaration of Helsinki and International Council for Harmonisation guidelines for Good Clinical Practice.

End points and assessments

The primary end point was mean change from baseline in AN count at week 16. The key secondary end point was the percentage of patients achieving ≥50% reduction from baseline in AN count with no increase in the number of abscesses or draining tunnels (HS Clinical Response [HiSCR]) at week 16. Other efficacy end points included percentage of patients achieving HiSCR at weeks 2 to 12, mean change from baseline at each visit in draining tunnel count, and percentage of patients experiencing ≥1 HS flare (≥25% increase in AN count [minimum increase of 2] from baseline). To further explore depth of responses, we also measured percentage of patients achieving ≥75%, ≥90%, and 100% reduction in AN count with no increase in the number of abscesses or draining tunnels (HiSCR75, HiSCR90, and HiSCR100) and percentage of patients achieving ≥55%, ≥75%, ≥90%, and 100% reduction in International Hidradenitis Suppurativa Severity Score System (IHS4-55, IHS4-75, IHS4-90, and IHS4-100) at each visit. IHS4 is a dynamic measure of HS severity calculated as the weighted sum of the number of inflammatory nodules (×1), abscesses (×2), and draining tunnels (×4).[27] IHS4-55 has been validated as a dichotomous version of IHS4.[28] Patients with missing postbaseline values at a scheduled visit were imputed as nonresponders at the visit for the dichotomous HiSCR- and IHS4-related end points.

Data as observed were used for all dichotomous end points associated with patient-reported outcomes. Patient-reported QoL questionnaires were answered at baseline and weeks 4, 8, and 16. Outcomes included mean change from baseline in the Hidradenitis Suppurativa Quality of Life (HiSQoL) questionnaire,[29,30] percentage of patients (with baseline score ≥4) achieving ≥4-point improvement in Dermatology Life Quality Index (DLQI),[31,32] and percentage of patients (with baseline score ≤48) achieving ≥4-point improvement in Functional Assessment of Chronic Illness Therapy—Fatigue (FACIT-F)[33] scores over time.

Skin Pain numerical rating scale (NRS) and Itch NRS were reported daily through week 16. Skin pain was assessed by the percentage of patients achieving Skin Pain NRS30 (≥30% and ≥1-unit reduction in Skin Pain NRS) and calculated among those with NRS ≥3 at baseline. Among patients with Itch NRS ≥4 at baseline, itch was evaluated by the percentage of patients achieving Itch NRS4, defined as a ≥4-point change relative to baseline.[34]

Physical examination, clinical laboratory tests, and vital sign assessments were also performed.

Statistical analysis

The planned sample size was 200 patients, based on a 2-sample *t* test for primary efficacy end point comparison. The mean change from baseline in AN count at week 16 was assumed to be −10 for the povorcitinib 45-mg or 75-mg groups and −6 for placebo, and a common SD was assumed to be 8, based on results from a previous study.[26] Using a 2-sided alpha of 0.1, 50 patients per group would have ≥80% power to detect a difference between either one of the highest povorcitinib dose groups and placebo. The planned sample size would also have ≥80% power to detect a significant HiSCR difference between either one of the highest povorcitinib dose groups and placebo at week 16 with 2-sided alpha of 0.1 by assuming response rates of 55% for the 45-mg or 75-mg groups and 30% for the placebo group using a Chi-square test.

All randomized patients were included in the intent-to-treat population used for the summary of demographics, baseline characteristics, patient disposition, and efficacy analyses. The safety population included all patients who received ≥1 dose of povorcitinib or placebo during the placebo-controlled period.

All analyses are presented through 16 weeks of double-blind, placebo-controlled treatment. Mean change from baseline in AN count at week 16 was assessed via mixed model repeated measures with the fixed effect of treatment group, Hurley stage (I, II, or III), geographic region (North America or Europe), visit, and treatment by visit interaction, and covariates of baseline measurement and baseline measurement by visit interaction. Comparisons

between each povorcitinib group and placebo were based on the least squares mean (SE). For HiSCR and IHS4-55 at each visit, logistic regression was used to compare each povorcitinib group versus placebo, whereas exact logistic regression was used for HiSCR75/HiSCR90/HiSCR100 and IHS4-75/IHS4-90/IHS4-100 at each visit. Both logistic and exact logistic regression models included treatment group, disease severity, and geographic region. Patient-reported outcomes were exploratory, and no statistical comparisons were performed.

RESULTS

Patients

Of 209 randomized patients (placebo, n = 52; povorcitinib 15 mg, n = 52; 45 mg, n = 52; 75 mg, n = 53), 207 (99.0%) were treated, and 174 (83.3%) completed the 16-week placebo-controlled period (Supplementary Fig 2, available via Mendeley at https://data.mendeley.com/datasets/hpc4rpv6j8/1).

Baseline demographics are shown in Table I and Supplementary Table I (available via Mendeley at https://data.mendeley.com/datasets/hpc4rpv6j8/1). Most patients were women (75.6%), White (70.3%), and non-Hispanic/Latino (85.6%), with a mean (SD) age of 37.1 (11.1) years. Mean (SD) body mass index was 35.7 (8.9) kg/m^2, and body mass indexes between 30 and <40 kg/m^2 were most common (44.5%). Over two-thirds (69.9%) of patients had Hurley II disease stage, and mean (SD) time since HS diagnosis was 10.3 (9.2) years. Mean (SD) baseline AN and draining tunnel counts were 11.6 (8.5) and 2.1 (3.9), respectively. Nearly half (45.9%) of patients had ≥1 draining tunnel. Prior treatment for HS consisted primarily of oral antibiotics (57.4%), with 18.2% previously treated with adalimumab and 5.7% with other biologics. Of the 205 patients with available data, 26.8% and 6.3% reported using analgesics and opioids for pain control, respectively.

Clinical efficacy

At week 16, the least squares mean (SE) change from baseline in AN count was −5.2 (0.9), −6.9 (0.9), and −6.3 (0.9) for povorcitinib 15, 45, and 75 mg, respectively, versus −2.5 (0.9) for placebo (Fig 1). Reductions from baseline in AN count were observed as early as week 2. Changes in AN count at week 16 for all povorcitinib doses versus placebo were statistically significant (15 mg, P = .0277; 45 mg, P = .0006; 75 mg, P = .0021).

More povorcitinib-treated patients achieved HiSCR at week 16 at the 15-mg (48.1%), 45-mg (44.2%), and 75-mg (45.3%) doses versus placebo (28.8%; P = .0445, P = .0998, and P = .0829, respectively; Fig 2). The placebo-adjusted difference in HiSCR for povorcitinib 15, 45, and 75 mg at time points between weeks 2 and 16 ranged from 7.7% to 19.2%, 15.4% to 30.8%, and 16.4% to 35.5%, respectively, suggesting superior clinical benefit for the higher doses. A numerically larger percentage of patients receiving any dose of povorcitinib also achieved HiSCR75/HiSCR90/HiSCR100 throughout the study (Supplementary Fig 3, available via Mendeley at https://data.mendeley.com/datasets/hpc4rpv6j8/1). Similar trends were observed for IHS4-55/IHS4-75/IHS4-90/IHS4-100 (Supplementary Fig 4, available via Mendeley at https://data.mendeley.com/datasets/hpc4rpv6j8/1).

During the study, a numerically lower percentage of patients treated with povorcitinib experienced ≥1 flare (15 mg, 25.0%; 45 mg, 21.6%; 75 mg, 17.0%) versus placebo (41.2%). At week 16, the mean (SD) change from baseline in draining tunnel counts in the overall population was +0.1 (3.3), −0.8 (3.2), and −1.1 (2.6) for povorcitinib 15, 45, and 75 mg, respectively, versus −0.3 (2.1) for placebo. Among patients with ≥3 draining tunnels at baseline, improvements were greater for povorcitinib (15 mg, −1.5 [4.6], n = 10; 45 mg, −3.2 [5.1], n = 12; 75 mg, −3.9 [3.8], n = 12) versus placebo (−1.1 [3.7], n = 12).

Patient-reported outcomes

At week 16, mean (SD) change from baseline in HiSQoL total score for povorcitinib 15, 45, and 75 mg was −4.0 (12.3), −9.1 (15.2), and −8.3 (17.9), respectively, versus −4.0 (14.0) for placebo. Among patients with baseline DLQI scores ≥4, 35.0%, 51.3%, and 63.2% of patients receiving povorcitinib 15, 45, and 75 mg and 34.2% of placebo-treated patients achieved a ≥4-point reduction in DLQI score at week 16. A ≥4-point improvement (increase) in FACIT-F score at week 16 in patients with FACIT-F scores ≤48 at baseline was achieved by 31.6%, 61.1%, and 47.6% of patients receiving povorcitinib 15, 45, and 75 mg, respectively, versus 34.2% for placebo.

Rates of Skin Pain NRS30 at week 16 among patients with Skin Pain NRS ≥3 at baseline were 44.1%, 51.5%, and 53.3% for povorcitinib 15, 45, and 75 mg, respectively, versus 30.8% for placebo-treated patients (Fig 3). Of patients with Itch NRS ≥4 at baseline, the percentage who had a ≥4-point reduction from baseline in Itch NRS at week 16 was 0%, 33.3%, and 42.3% for povorcitinib 15, 45, and 75 mg versus 15.0% for placebo (Supplementary Fig 5, available via Mendeley at https://data.mendeley.com/datasets/hpc4rpv6j8/1).

Table I. Key patient demographics and clinical characteristics at baseline

Characteristic	Placebo (*n* = 52)	Povorcitinib 15 mg (*n* = 52)	Povorcitinib 45 mg (*n* = 52)	Povorcitinib 75 mg (*n* = 53)	Total (*N* = 209)
Age, mean (SD), y	35.2 (10.0)	38.2 (10.9)	37.3 (12.5)	37.5 (10.8)	37.1 (11.1)
Women, *n* (%)	43 (82.7)	37 (71.2)	39 (75.0)	39 (73.6)	158 (75.6)
Race, *n* (%)					
White	40 (76.9)	36 (69.2)	35 (67.3)	36 (67.9)	147 (70.3)
Black	10 (19.2)	13 (25.0)	12 (23.1)	16 (30.2)	51 (24.4)
Asian	1 (1.9)	2 (3.8)	2 (3.8)	1 (1.9)	6 (2.9)
Other*	1 (1.9)	1 (1.9)	3 (5.8)	0	5 (2.4)
Time since diagnosis, mean (SD), y	8.1 (6.5)	9.9 (8.1)	11.2 (11.5)	12.1 (9.7)	10.3 (9.2)
HS family history, *n* (%)	12 (23.1)	9 (17.3)	15 (28.8)	15 (28.3)	51 (24.4)
BMI, mean (SD), kg/m^2	34.1 (9.0)	35.0 (8.1)	36.8 (9.6)	37.1 (8.6)	35.7 (8.9)
Selected comorbidities, *n* (%)					
Depression	17 (32.7)	14 (26.9)	15 (28.8)	14 (26.4)	60 (28.7)
Anxiety	12 (23.1)	15 (28.8)	13 (25.0)	11 (20.8)	51 (24.4)
Gastrointestinal disorders	12 (23.1)	8 (15.4)	13 (25.0)	14 (26.4)	47 (22.5)
Hypertension	6 (11.5)	12 (23.1)	13 (25.0)	12 (22.6)	43 (20.6)
Diabetes	4 (7.7)	8 (15.4)	10 (19.2)	4 (7.5)	26 (12.4)
Anemia	5 (9.6)	3 (5.8)	5 (9.6)	3 (5.7)	16 (7.7)
Smoking history, *n* (%)					
Current	21 (40.4)	24 (46.2)	25 (48.1)	21 (39.6)	91 (43.5)
Former	7 (13.5)	6 (11.5)	8 (15.4)	9 (17.0)	30 (14.4)
Hurley stage, *n* (%)					
I	4 (7.7)	3 (5.8)	4 (7.7)	4 (7.5)	15 (7.2)
II	36 (69.2)	37 (71.2)	36 (69.2)	37 (69.8)	146 (69.9)
III	12 (23.1)	12 (23.1)	12 (23.1)	12 (22.6)	48 (23.0)
AN count, mean (SD)	11.2 (5.9)	11.8 (7.1)	12.9 (12.3)	10.6 (7.2)	11.6 (8.5)
Draining tunnel count, mean (SD)	2.4 (4.0)	2.3 (4.4)	2.2 (4.0)	1.6 (2.9)	2.1 (3.9)
IHS4 score, mean (SD)	22.9 (17.0)	22.4 (23.2)	23.5 (22.8)	18.9 (17.3)	21.9 (20.2)
Previous HS treatments, *n* (%)					
Oral antibiotics	35 (67.3)	26 (50.0)	29 (55.8)	30 (56.6)	120 (57.4)
Topical antibiotics	20 (38.5)	12 (23.1)	15 (28.8)	14 (26.4)	61 (29.2)
Topical antiseptics	10 (19.2)	10 (19.2)	14 (26.9)	8 (15.1)	42 (20.1)
Adalimumab	7 (13.5)	8 (15.4)	14 (26.9)	9 (17.0)	38 (18.2)
Incision and drainage	5 (9.6)	6 (11.5)	6 (11.5)	12 (22.6)	29 (13.9)
Surgery	10 (19.2)	10 (19.2)	4 (7.7)	8 (15.1)	32 (15.3)
Other biologics	5 (9.6)	4 (7.7)	3 (5.8)	0	12 (5.7)
Treatment-naive	3 (5.8)	5 (9.6)	5 (9.6)	3 (5.7)	16 (7.7)

AN, Abscess and inflammatory nodule; *BMI*, body mass index; *HS*, hidradenitis suppurativa; *IHS4*, International Hidradenitis Suppurativa Severity Score System.
*Includes one patient who identified as American Indian/Alaska Native and 4 who identified as *other*.

Safety

In total, 60.0% of povorcitinib-treated (15 mg, 59.6%; 45 mg, 60.0%; 75 mg, 60.4%) and 65.4% of placebo-treated patients reported a treatment-emergent adverse event (TEAE; Table II). Treatment-related TEAEs occurred in 21.3% of patients receiving any povorcitinib dose (15 mg, 17.3%; 45 mg, 24.0%; 75 mg, 22.6%) and 23.1% with placebo.

Discontinuations due to TEAEs occurred in 5 placebo-treated and 4 povorcitinib-treated patients (15 mg, *n* = 2; 45 mg, *n* = 2). No fatal TEAEs occurred. Grade ≥3 infection incidence was observed in 2 patients (1 each in the placebo and povorcitinib 15-mg groups). Two patients (1 each in the placebo and povorcitinib 45-mg groups) discontinued study treatment due to TEAEs of infection. No cases of herpes zoster were reported. Acne was observed in 7 patients (4.5%) receiving povorcitinib (all grade 1/2), although 13.4% overall reported a history of acne. The most common select laboratory abnormality during the placebo-controlled period in patients

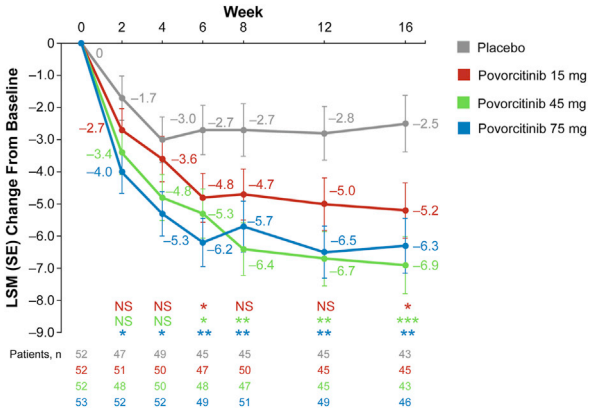

Fig 1. Change from baseline in abscess and inflammatory nodule count. Evaluated in the intent-to-treat population with missing postbaseline values handled using the mixed model repeated measures missing-at-random assumption. *$P < .05$; **$P < .01$; ***$P < .001$. *P* values versus placebo. *LSM*, Least squares mean; *NS*, not statistically significant.

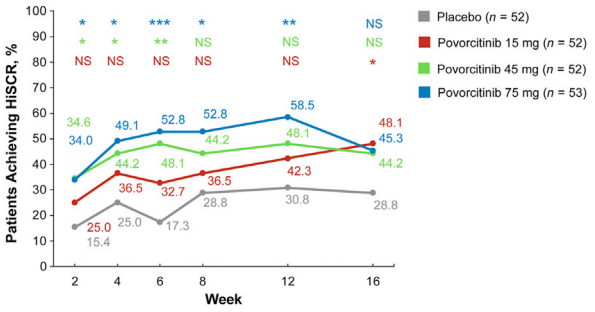

Fig 2. Percentage of patients achieving HiSCR over time. Evaluated in the intent-to-treat population with missing postbaseline values handled using nonresponder imputation. *$P < .05$; **$P < .01$; ***$P < .001$. *P* values versus placebo. *AN*, Abscess and inflammatory nodule; *dT*, draining tunnel; *HiSCR*, Hidradenitis Suppurativa Clinical Response (≥50% decrease from baseline in AN count with no increase in the number of abscesses or draining tunnels); *NS*, not statistically significant.

treated with povorcitinib was blood creatine phosphokinase elevation (6 patients, 5.6%); however, no symptoms of myositis or rhabdomyolysis were observed. No patients had platelet counts <100 × 10^9/L; other laboratory parameter abnormalities were generally infrequent.

Five serious adverse events (SAEs) occurred in 3 patients receiving povorcitinib (fall and rib fracture [15 mg]; herniated disc [45 mg]; pulmonary embolism and pneumonia [15 mg]), and 4 SAEs occurred in 3 patients receiving placebo (cholecystitis; limb abscess and bacterial infection; atrial fibrillation); no SAEs were reported for the 75-mg group. The only SAEs considered potentially related to treatment occurred in the same patient (grade 3 pneumonia

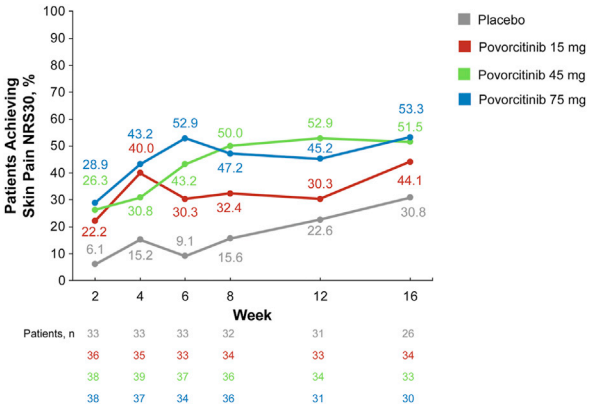

Fig 3. Percentage of patients with baseline Skin Pain NRS ≥3 achieving skin pain NRS30 over time. Statistical testing was not performed, and data were reported as observed. *NRS*, Numerical rating scale; NRS30, ≥30% reduction and ≥1-unit reduction from baseline in NRS.

and pulmonary embolism [15 mg]); this patient had risk factors for pulmonary embolism (Supplementary Safety Narrative, available via Mendeley at https://data.mendeley.com/datasets/hpc4rpv6j8/1).

DISCUSSION

In this phase 2 study in patients with HS, the oral JAK1-selective inhibitor povorcitinib was effective, resulting in significantly decreased AN counts, reduced draining tunnel counts, higher percentages of patients achieving HiSCR and IHS4-55 (reaching statistical significance for most study visits in the 75-mg group), and fewer HS flares versus placebo (Supplementary Table II, available via Mendeley at https://data.mendeley.com/datasets/hpc4rpv6j8/1). Clinical responses appeared higher at week 12, with some reduction in the percentage of patients achieving HiSCR and IHS4-55 at week 16, which may reflect the natural fluctuations in HS lesion counts observed in other clinical trials.[11,35-37] Additional analyses with larger patient populations will be needed to determine povorcitinib efficacy over time. Importantly, decreases in lesion count observed with povorcitinib were evident by week 2, and response depth was high in some patients, as shown with the more stringent end points HiSCR75/90/100 and IHS4-75/90/100.

The patient-reported outcomes HiSQoL, DLQI, FACIT-F, Skin Pain NRS, and Itch NRS supported the efficacy of 45- and 75-mg povorcitinib doses. Skin pain and itch improvements with povorcitinib were rapid, including for patients with the highest baseline scores. These results are particularly important, considering that pain is the most common and disabling symptom of HS.[3] Povorcitinib was

Table II. Summary of treatment-emergent adverse events

Event, *n* (%)	Placebo (*n* = 52)	Povorcitinib 15 mg (*n* = 52)	Povorcitinib 45 mg (*n* = 50)	Povorcitinib 75 mg (*n* = 53)	Total povorcitinib (*N* = 155)
Any TEAEs	34 (65.4)	31 (59.6)	30 (60.0)	32 (60.4)	93 (60.0)
Grade ≥3	3 (5.8)	2 (3.8)	2 (4.0)	1 (1.9)	5 (3.2)
SAEs	3 (5.8)	2 (3.8)	1 (2.0)	0	3 (1.9)
Discontinued due to TEAEs	5 (9.6)	2 (3.8)	2 (4.0)	0	4 (2.6)
Any treatment-related TEAEs	12 (23.1)	9 (17.3)	12 (24.0)	12 (22.6)	33 (21.3)
Grade ≥3	0	1 (1.9)	1 (2.0)	1 (1.9)	3 (1.9)
SAEs	0	1 (1.9)	0	0	1 (0.6)
Most frequently occurring TEAEs*					
Fatigue	4 (7.7)	4 (7.7)	5 (10.0)	6 (11.3)	15 (9.7)
Headache	5 (9.6)	4 (7.7)	2 (4.0)	4 (7.5)	10 (6.5)
Diarrhea	1 (1.9)	3 (5.8)	2 (4.0)	3 (5.7)	8 (5.2)
Nausea	5 (9.6)	3 (5.8)	2 (4.0)	3 (5.7)	8 (5.2)
Infections					
Upper respiratory tract infection	2 (3.8)	0	1 (2.0)	4 (7.5)	5 (3.2)
Fungal infection	0	1 (1.9)	1 (2.0)	2 (3.8)	4 (2.6)
Urinary tract infection	1 (1.9)	0	1 (2.0)	3 (5.7)	4 (2.6)
Grade ≥3	1 (1.9)	1 (1.9)	0	0	1 (0.6)
Leading to discontinuation	1 (1.9)	0	1 (2.0)	0	1 (0.6)
Acne	0	1 (1.9)	3 (6.0)	3 (5.7)	7 (4.5)
Laboratory abnormalities†					
Platelet count $<100\times10^9$/L	0	0	0	0	0
Hemoglobin ≤9.0 g/dL	1 (2.0)	1 (1.9)	0	1 (1.9)	2 (1.3)
Neutrophils $<1.0\times10^9$/L	0	0	1 (2.0)	1 (1.9)	2 (1.3)
AST ≥3 × ULN	0	1 (1.9)	3 (6.0)	0	4 (2.6)
ALT ≥3 × ULN	0	1 (1.9)	1 (2.0)	1 (1.9)	3 (1.9)
CPK ≥5 × ULN‡	0	1 (2.6)	3 (9.4)	2 (5.3)	6 (5.6)

ALT, Alanine aminotransferase; *AST*, aspartate aminotransferase; *CPK*, creatine phosphokinase; *SAE*, serious adverse event; *TEAE*, treatment-emergent adverse event; *ULN*, upper limit of normal.
*Events occurring in ≥5% of patients overall are shown.
†Except for CPK, laboratory assessments were performed for 51 placebo patients.
‡CPK analyses were conducted for a smaller number of patients: placebo, *n* = 34; povorcitinib 15 mg, *n* = 38; 45 mg, *n* = 32; 75 mg, *n* = 38 (total number of patients treated with povorcitinib with CPK results was 108).

generally well tolerated at all doses tested, with no trends in TEAE incidence or severity observed with increasing doses.

Limitations of this phase 2 study include relatively small sample sizes and minor imbalance of baseline AN and draining tunnel counts among treatment arms.

In conclusion, povorcitinib demonstrated rapid clinical efficacy for HS, with no evidence of increased risk of AEs across doses evaluated. Povorcitinib was also associated with numerical improvements in QoL, including in patient-reported skin pain, itch, and fatigue. These promising results support further evaluation of the efficacy and safety of povorcitinib in the ongoing phase 3 registrational studies of patients with moderate to severe HS (STOP-HS1, NCT05620823; STOP-HS2, NCT05620836).

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Conflicts of interest

Dr Kirby has served as a speaker for AbbVie and as a consultant for AbbVie, Bayer, ChemoCentryx, Incyte Corporation, InflaRx, Janssen, Novartis, Pfizer, and UCB. Dr Okun is a consultant for AbbVie, Azora, Bluefin, Boehringer Ingelheim, ChemoCentryx, Incyte, InflaRx, Innovaderm, Novartis, Pfizer, and Vyne. Dr Alavi received honoraria as a consultant or advisory board participant from AbbVie, InflaRx, Incyte, Novartis, Boehringer Ingelheim, and UCB and received honoraria as an

investigator for Boehringer Ingelheim and Processa. Dr Bechara has received honoraria for participation in advisory boards, in clinical trials, and/or as a speaker from AbbVie, AbbVie Deutschland, Boehringer Ingelheim, Incyte, Janssen-Cilag, MoonLake, Novartis, and UCB. Dr Zouboulis declares that none of the mentioned conflicts of interest had any influence on this manuscript. He reports consultancy/advisory board disease-relevant honoraria from Boehringer Ingelheim, Incyte, InflaRx, Janssen-Cilag, Novartis, Regeneron, Sanofi, UCB, and Viatris. He has received speaker fees from Almirall, Novartis, and UCB; is President of the EHSF eV, coordinator of the ALLOCATE Skin group of the ERN Skin and chair of the ARHS Task Force group of the EADV. He is Editor of the EADV News; is cocopyright holder of IHS4 on behalf of the EHSF eV. His employer has received disease-relevant grants from Boehringer Ingelheim, InflaRx, Novartis, and UCB for his participation as clinical investigator. Dr Bibeau was an employee of Incyte at the time of the study. Drs Brown, Santos, and Wang are employees and shareholders of Incyte. Dr Kimball's institution has received grants from AbbVie, Admirx, AnaptysBio, Aristea, Bristol Myers Squibb, Eli Lilly, Incyte, Janssen, MoonLake, Novartis, Pfizer, Prometheus, UCB, and Sonoma Bio, fellowship funding from Janssen and AbbVie. She received consulting fees from AbbVie, Alumis, Bayer, Boehringer Ingelheim, Eli Lilly, Evommune, Janssen, MoonLake, Novartis, Pfizer, Priovant, Sonoma Bio, Sanofi, UCB, and Target RWE, and serves on the board of directors of Almirall. Dr Porter is a consultant and/or investigator for AbbVie, Acelyrin, Alumis, AnaptysBio, Aristea, Bayer, Bristol Myers Squibb, Eli Lilly, Incyte, Janssen, MoonLake, Novartis, Pfizer, Prometheus Laboratories, Regeneron, Sanofi, Trifecta Clinical, Sonoma Bio, and UCB.

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JAAD Game changer

JAAD Game Changer: Quality of life in adults with facial port-wine stains

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How did this article change the practice of dermatology?

- As a dermatologist, it is important to treat the whole person because many skin conditions affect more than just the skin. In patients with port-wine stains, providers should inquire about the quality of life and provide patients with appropriate support and resources to deal with some of these issues.

Conflicts of interest: None disclosed.

Note: A Game Changer is a short narrative stating how an article that originally appeared in *JAAD* changed the game of dermatology. The Game Changer author is not the author of the original article.

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