P0004

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Efficacy and Safety of the Janus Kinase 1 Inhibitor Povorcitinib (INCB054707) in Patients With Hidradenitis Suppurativa: Results From a Randomized, Placebo-Controlled, Phase 2 Dose-Ranging Study

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Background

- Hidradenitis suppurativa (HS) is a chronic, debilitating inflammatory condition characterized by painful nodules and abscesses that can lead to tunnels and scarring[1]
- Current standard-of-care medical therapies for HS consist of topical or systemic antibiotics, used across the spectrum of disease severity, and immunomodulatory and biologic therapy, which are recommended for moderate or severe disease[2,3]
  - Other treatments include hormonal therapies, which may be used as monotherapy for female patients with mild to moderate HS or as add-on treatment for more severe disease, and retinoids[2,3]
- Dysregulation of the Janus kinase (JAK)/signal transducer and activator of transcription (STAT) pathway is involved in a wide variety of inflammatory disorders, including HS[4]
- Povorcitinib (INCB054707) is an oral, JAK1-selective, small-molecule inhibitor that demonstrated proof of concept over 8 weeks of treatment in two phase 2 studies in moderate to severe HS[5]; doses of 30 mg, 60 mg, and 90 mg were generally well tolerated, with no serious adverse events (AEs)

Objective

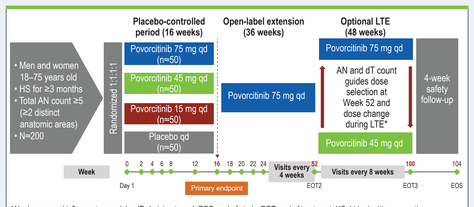
- To evaluate the efficacy and safety results of povorcitinib in a randomized, placebo-controlled, phase 2 dose-ranging study of povorcitinib over 16 weeks of treatment (NCT04476043; EudraCT 2020-001981-13)

Methods

Patients and Study Design

- Eligible patients were men and women aged 18–75 years, with HS (Hurley stage I, II, or III) for ≥3 months before screening (**Figure 1**)
  - Diagnosis of HS was defined as total abscess and inflammatory nodule (AN) count ≥5 in ≥2 distinct anatomic areas at screening and baseline
- Patients were excluded if they had >20 draining tunnels, decreased blood cell counts at screening (leukocytes <3.0 × 10^9/L, absolute neutrophil count <1.5 × 10^9/L, lymphocytes <0.8 × 10^9/L, hemoglobin <9 g/dL, or platelet count <150 × 10^9/L), had previously failed to respond to any JAK inhibitor, or had used immunomodulating biologic drugs within 12 weeks (or 5 half-lives)
- Patients were randomized (1:1:1:1) to receive 1 of 3 doses of povorcitinib (15, 45, or 75 mg) or placebo once daily for 16 weeks of double-blind treatment

Figure 1. Study Design



AN, abscess and inflammatory nodule; dT, draining tunnel; EOS, end of study; EOT, end of treatment; HS, hidradenitis suppurativa; LTE, long-term extension; qd, once daily.
* For the initial dose, patients with AN and dT counts ≤2 and >2 received povorcitinib 45 mg qd and 75 mg qd (or the last dose dispensed during the LTE), respectively. Subsequent doses were based on the AN and dT counts at each visit: patients with counts >5 received povorcitinib 75 mg qd; dosing was decreased or maintained at 45 mg qd for counts ≤2.

Endpoints and Assessments

- The primary endpoint was mean change from baseline in AN count at Week 16
- Secondary endpoints included
  - Mean change from baseline in AN count
  - Percentage of patients achieving HS Clinical Response (HiSCR or HiSCR75; ≥50% or ≥75% decrease from baseline in AN count with no increase in number of abscesses or draining tunnels, respectively)
  - Mean change from baseline in International Hidradenitis Suppurativa Severity Score System (IHS4)
  - Mean change from baseline in draining tunnel count through Week 16
- Safety was assessed by the frequency and severity of treatment-emergent AEs (TEAEs)

Statistical Analysis

- All analyses are presented through 16 weeks of placebo-controlled, double-blind treatment
- All randomized patients were included in the intent-to-treat (ITT) population, which was used for all efficacy data
- The safety population included all patients who received ≥1 dose of povorcitinib or placebo during the placebo-controlled period
- Mean change from baseline in AN count and IHS4 were assessed via mixed model repeated measures in the ITT population
  - The study was powered to detect a mean change from baseline in AN count of –10 for the 45-mg and 75-mg treatment groups and –6 for the placebo group; using a 2-sided alpha of 0.1, 50 patients per group would give ≥80% power to detect such a difference
- Statistical comparisons for HiSCR at Week 16 in the ITT population were tested using logistic regression, which included treatment group, stratification factors (disease severity based on Hurley stage), and geographic region
- All other secondary outcomes were summarized using descriptive statistics

Results

Patients

- In total, 209 patients were randomized (placebo, n=52; povorcitinib, n=157 [15 mg, n=52; 45 mg, n=52; 75 mg, n=53]; **Table 1**); baseline demographics and clinical characteristics were generally typical for patients with HS[6]
  - Median (range) age was 36 (19–70) years
  - Median (range) body mass index was 35.0 (19.8–66.6) kg/m^2
  - 81.8% of patients were from North America
  - 75.6% were women
  - 70.3% were White, 24.4% were Black/African American, and 2.9% were Asian
  - 57.9% were current or former smokers
- At baseline, 69.9% of patients were Hurley stage II, and 23.0% were Hurley stage III
  - Median (range) disease duration was 7.2 (0.1–48.4) years
  - Mean (SD) AN count was 11.6 (8.5), and mean draining tunnel count was 2.1 (3.9)
    - Mean (SD) abscess count was 1.8 (2.9), and mean inflammatory nodule count was 9.8 (8.1)
  - Mean (SD) IHS4 was 21.9 (20.2)

Table 1. Patient Demographics and Baseline Clinical Characteristics

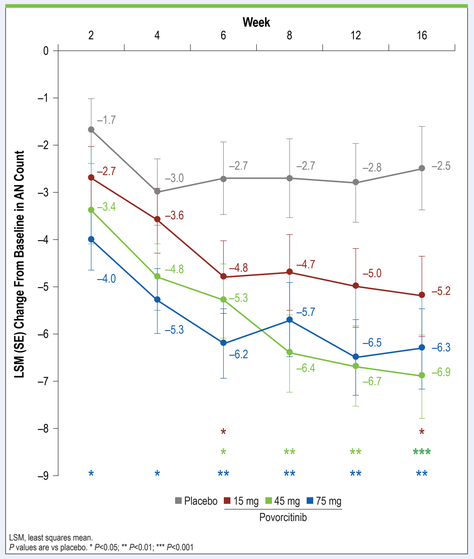
Characteristic	Placebo (n=52)	Povorcitinib 15 mg (n=52)	Povorcitinib 45 mg (n=52)	Povorcitinib 75 mg (n=53)	Total (N=209)
Age, median (range), y	33.5 (21–65)	36.5 (21–70)	35.0 (19–66)	38.0 (19–65)	36.0 (19–70)
Women, n (%)	43 (82.7)	37 (71.2)	39 (75.0)	39 (73.6)	158 (75.6)
Race, n (%)					
White	40 (76.9)	36 (69.2)	35 (67.3)	36 (67.9)	147 (70.3)
Black/African American	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)*
Ethnicity, n (%)					
Hispanic or Latino	10 (19.2)	5 (9.6)	7 (13.5)	6 (11.3)	28 (13.4)
Not Hispanic or Latino	41 (78.8)	47 (90.4)	44 (84.6)	47 (88.7)	179 (85.6)
Unknown/Other	1 (1.9)	0	1 (1.9)	0	2 (1.0)
Geographic region, n (%)					
North America	43 (82.7)	42 (80.8)	43 (82.7)	43 (81.1)	171 (81.8)
Europe	9 (17.3)	10 (19.2)	9 (17.3)	10 (18.9)	38 (18.2)
BMI, median (range), kg/m^2	34.3 (20.2–60.6)	34.6 (19.8–52.9)	35.1 (21.6–66.6)	36.5 (22.8–61.2)	35.0 (19.8–66.6)
≥30 kg/m^2	34 (65.4)	38 (73.1)	41 (78.8)	43 (81.1)	156 (74.6)
HS family history, n (%)	12 (23.1)	9 (17.3)	15 (28.8)	15 (28.3)	51 (24.4)
Smoking history, n (%)					
Never	24 (46.2)	22 (42.3)	19 (36.5)	23 (43.4)	88 (42.1)
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)
Select comorbidities, n (%)					
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)
Psoriasis	4 (7.7)	1 (1.9)	1 (1.9)	1 (1.9)	7 (3.3)
Previous HS treatments, n (%)†					
Treatment-naive	3 (5.8)	5 (9.6)	5 (9.6)	3 (5.7)	16 (7.7)
Topical antiseptics	10 (19.2)	10 (19.2)	14 (26.9)	8 (15.1)	42 (20.1)
Topical antibiotics	20 (38.5)	12 (23.1)	15 (28.8)	14 (26.4)	61 (29.2)
Oral antibiotics	35 (67.3)	26 (50.0)	29 (55.8)	30 (56.6)	120 (57.4)
Adalimumab	7 (13.5)	8 (15.4)	14 (26.9)	9 (17.0)	38 (18.2)
Other biologics	5 (9.6)	4 (7.7)	3 (5.8)	0	12 (5.7)
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)
Disease duration, mean (SD), y	8.1 (6.5)	9.9 (8.1)	11.2 (11.5)	12.1 (9.7)	10.3 (9.2)
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)
Abscess count, mean (SD)	2.0 (3.0)	1.4 (2.9)	1.8 (2.7)	2.1 (3.0)	1.8 (2.9)
Inflammatory nodule count, mean (SD)	9.1 (5.4)	10.4 (6.8)	11.1 (11.8)	8.6 (7.1)	9.8 (8.1)
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, mean (SD)	22.9 (17.0)	22.4 (23.2)	23.5 (22.8)	18.9 (17.3)	21.9 (20.2)

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; † Treatments reported in >15% of patients are shown.

Efficacy

- At Week 16, patients receiving povorcitinib had significantly greater decreases from baseline in AN count (least squares mean [LSM; SE] change, 15 mg, −5.2 [0.9], *P*=0.0277; 45 mg, −6.9 [0.9], *P*=0.0006; 75 mg, −6.3 [0.9], *P*=0.0021) vs placebo (−2.5 [0.9]; **Figure 2**)

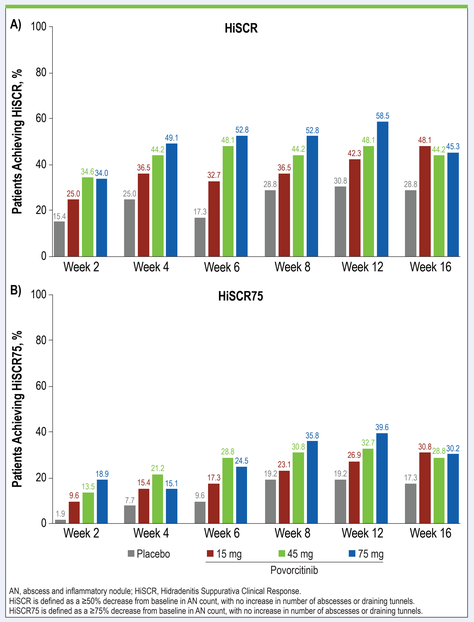
Figure 2. Change From Baseline in AN Count



LSM, least squares mean.
P values are vs placebo. * *P*<0.05; ** *P*<0.01; *** *P*<0.001

- At Week 16, a numerically greater percentage of patients receiving povorcitinib achieved HiSCR (15 mg, 48.1%; 45 mg, 44.2%; 75 mg, 45.3%) vs placebo (28.8%; **Figure 3A**)
- Similar findings were observed for patients achieving HiSCR75 at Week 16 (15 mg, 30.8%; 45 mg, 28.8%; 75 mg, 30.2%; placebo, 17.3%; **Figure 3B**)

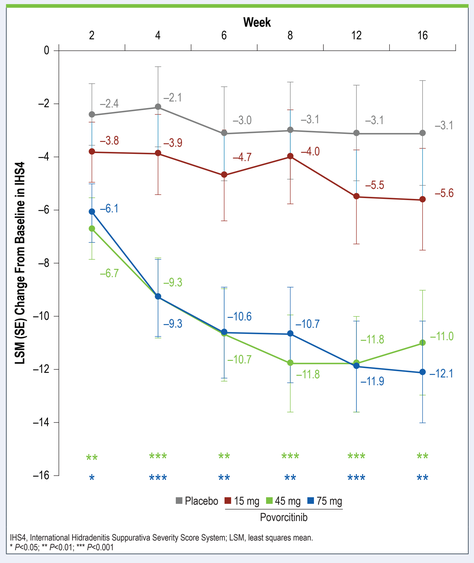
Figure 3. Patients Achieving (A) HiSCR or (B) HiSCR75



AN, abscess and inflammatory nodule; HiSCR, Hidradenitis Suppurativa Clinical Response.
HiSCR is defined as a ≥50% decrease from baseline in AN count, with no increase in number of abscesses or draining tunnels.
HiSCR75 is defined as a ≥75% decrease from baseline in AN count, with no increase in number of abscesses or draining tunnels.

- Dose-dependent decreases from baseline were seen in IHS4 at Week 16 with povorcitinib (**Figure 4**)

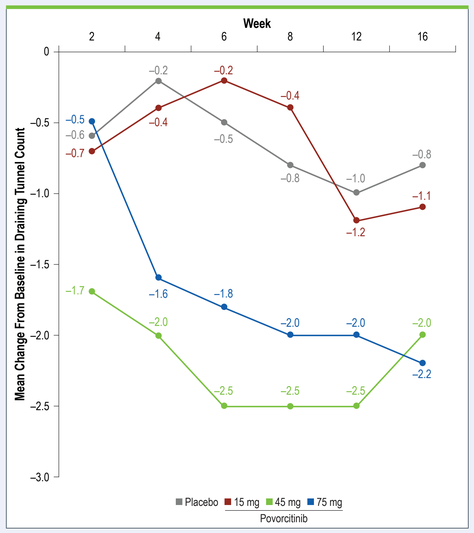
Figure 4. Change From Baseline in IHS4



IHS4, International Hidradenitis Suppurativa Severity Score System; LSM, least squares mean.
* *P*<0.05; ** *P*<0.01; *** *P*<0.001

- Among patients with a baseline draining tunnel count ≥1, povorcitinib decreased draining tunnel count at Week 16 (**Figure 5**)

Figure 5. Change From Baseline in Draining Tunnel Count



Safety

- In the safety-evaluable population (placebo, n=52; povorcitinib, n=155 [15 mg, n=52; 45 mg, n=50; 75 mg, n=53]), 65.4% of placebo- and 60.0% of povorcitinib-treated patients (15 mg, 59.6%; 45 mg, 60.0%; 75 mg, 60.4%) reported any TEAE (**Table 2**)
  - The most common TEAEs among povorcitinib-treated patients were fatigue (9.7%), headache (6.5%), diarrhea (5.2%), and nausea (5.2%)
- In total, 4 patients (2.6%) who received povorcitinib discontinued treatment, and 12 patients (7.7%) interrupted treatment due to a TEAE

Table 2. Most Common TEAEs

Events, n (%)	Placebo (n=52)	Povorcitinib 15 mg (n=52)	Povorcitinib 45 mg (n=50)	Povorcitinib 75 mg (n=53)	Total Povorcitinib (N=155)
Any TEAE*	34 (65.4)	31 (59.6)	30 (60.0)	32 (60.4)	93 (60.0)
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)
Acne	0	1 (1.9)	3 (6.0)	3 (5.7)	7 (4.5)
Nasopharyngitis	0	3 (5.8)	3 (6.0)	0	6 (3.9)
Vomiting	0	3 (5.8)	2 (4.0)	1 (1.9)	6 (3.9)
COVID-19	1 (1.9)	2 (3.8)	2 (4.0)	1 (1.9)	5 (3.2)
Constipation	2 (3.8)	4 (7.7)	0	1 (1.9)	5 (3.2)
Decreased appetite	0	1 (1.9)	2 (4.0)	2 (3.8)	5 (3.2)
Upper RTI	2 (3.8)	0	1 (2.0)	4 (7.5)	5 (3.2)

RTI, respiratory tract infection; TEAE, treatment-emergent adverse event.
* Events occurring in ≥5 patients treated with povorcitinib overall are shown.

- Grade ≥3 TEAEs occurred in 5.8% of patients receiving placebo and 3.2% of patients receiving povorcitinib (15 mg, 3.8%; 45 mg, 4.0%; 75 mg, 1.9%)
- Serious TEAEs occurred in 5.8% of patients receiving placebo and 1.9% of patients receiving povorcitinib (15 mg, 3.8%; 45 mg, 2.0%; 75 mg, 0%)
- Neutrophil count decrease and platelet count decrease were observed in 1 patient each (0.6%) treated with povorcitinib (both grade 1/2 at 75 mg); no patient treated with povorcitinib had an AE of hemoglobin decrease
- There were no fatal TEAEs
- In total, 21.3% of povorcitinib-treated patients reported any treatment-related AE (TRAE; **Table 3**)
  - The most common TRAEs were fatigue (4.5%), acne (2.6%), and headache (2.6%)

Table 3. Most Common TRAEs

Events, n (%)	Placebo (n=52)	Povorcitinib 15 mg (n=52)	Povorcitinib 45 mg (n=50)	Povorcitinib 75 mg (n=53)	Total Povorcitinib (N=155)
Any TRAE*	12 (23.1)	9 (17.3)	12 (24.0)	12 (22.6)	33 (21.3)
Fatigue	1 (1.9)	2 (3.8)	3 (6.0)	2 (3.8)	7 (4.5)
Acne	0	0	2 (4.0)	2 (3.8)	4 (2.6)
Headache	4 (7.7)	1 (1.9)	2 (4.0)	1 (1.9)	4 (2.6)
CPK increased	0	0	1 (2.0)	2 (3.8)	3 (1.9)
Nausea	5 (9.6)	1 (1.9)	0	2 (3.8)	3 (1.9)
Contusion	1 (1.9)	0	0	2 (3.8)	2 (1.3)
Nasopharyngitis	0	0	2 (4.0)	0	2 (1.3)
Vomiting	0	0	1 (2.0)	1 (1.9)	2 (1.3)

CPK, creatine phosphokinase; TRAE, treatment-related adverse event.
* Events occurring in >1 patient treated with povorcitinib overall are shown.

Conclusions

- **Results from this phase 2 study of povorcitinib in patients with HS suggest a trend toward dose-dependent efficacy between 15 mg and the higher doses, with no evidence for increased risk of serious toxicity at higher doses**
- **The open-label extension period is ongoing and will provide further information on efficacy, safety, and tolerability with longer-term povorcitinib administration**

Disclosures

JSK has served as a speaker for AbbVie and as a consultant for AbbVie, Bayer, ChemoCentryx, Incyte, InflaRx, Janssen, Novartis, Pfizer, and UCB. MMO is a consultant for AbbVie, Azora, Bluefin, Boehringer Ingelheim, ChemoCentryx, Incyte, Innovaderm, InflaRx, Pfizer, and Vyne. AA received honoraria as a consultant or advisory board participant from AbbVie, Janssen, Novartis, Boehringer Ingelheim, InflaRx, and UCB; and received honoraria as an investigator for Boehringer Ingelheim and Processa. FGB has received honoraria for participation in advisory boards, in clinical trials, and/or as a speaker from AbbVie Inc., AbbVie Deutschland GmbH & Co. KG, Boehringer Ingelheim Pharma GmbH & Co. KG, Novartis Pharma GmbH, UCB Pharma, Incyte, and Janssen-Cilag GmbH. CCZ declares that none of the mentioned conflicts of interest had any influence on this poster. He reports consultancy/advisory board disease-relevant honoraria from AbbVie, Bayer, Incyte, InflaRx, Janssen-Cilag, Novartis, Regeneron, and UCB. He has received speaker fees from AbbVie and UCB; is President of the EHSF e.V., 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 co-copyright holder of IHS4 on behalf of the EHSF e.V. His employer has received disease-relevant grants from AbbVie, Boehringer Ingelheim, InflaRx, Novartis, and UCB for his participation as clinical investigator. KB, LLS, and AW are employees and shareholders of Incyte. ABK is a consultant and investigator for AbbVie, Bristol Myers Squibb, Eli Lilly, Janssen, Novartis, Pfizer, and UCB; investigator for AnaptysBio and Incyte; consultant for Bayer, Boehringer Ingelheim, Concert, EvolImmune, Moonlake, Sonoma Bio, and Ventyx; receives fellowship funding from AbbVie and Janssen; and serves on the Board of Directors for AImirall. MLP is a consultant and/or investigator for AbbVie, AnaptysBio, Eli Lilly, Incyte, Janssen, Novartis, Pfizer, Trifecta Clinical (in conjunction with Acelyrin, Moonlake, and Aristea), and UCB.

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