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Janus Kinase 1 Inhibition With Povorcitinib (INCB054707) in Hidradenitis Suppurativa: Efficacy and Safety During the Open-Label Extension Period of a Phase 2 Study

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Introduction

- Hidradenitis suppurativa (HS) is a chronic, inflammatory condition characterized by recurrent painful skin nodules and abscesses that can lead to draining tunnels, irreversible tissue damage, and scarring[1]
- Povorcitinib is an oral, small-molecule, selective Janus kinase 1 inhibitor
- Povorcitinib demonstrated dose-dependent efficacy in patients with HS in the 16-week, randomized, placebo-controlled, phase 2 dose-ranging study conducted in North America and Europe[2-4]

Objective

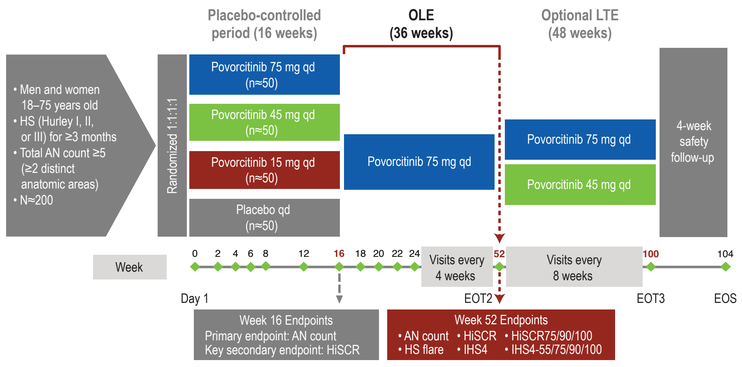
- To present efficacy and safety results for patients with HS treated with povorcitinib in the 36-week open-label extension (OLE) period following the 16-week, randomized, placebo-controlled period

Methods

Study Design and Patients

- This was a randomized, placebo-controlled phase 2 dose-ranging study evaluating the efficacy and safety of povorcitinib in adult patients with HS (**Figure 1**)
  - Patients were randomized 1:1:1:1 to receive 1 of 3 doses of povorcitinib (15, 45, or 75 mg) or placebo once daily (qd) for 16 weeks of double-blind treatment
  - Patients received povorcitinib 75 mg qd for the 36-week OLE period

Figure 1. Study Design (NCT04476043; EudraCT 2020-001981-13)



AN, abscess and inflammatory nodule; EOS, end of study; EOT, end of treatment; HiSCR, ≥50% reduction from baseline in AN count with no increase in the number of abscesses or draining tunnels (Hidradenitis Suppurativa Clinical Response); HiSCR75/90/100, ≥75%/90%/100% reduction from baseline in AN count with no increase in the number of abscesses or draining tunnels; HS, hidradenitis suppurativa; IHS4-55/75/90/100, ≥55%/75%/90%/100% reduction from baseline in the International Hidradenitis Suppurativa Severity Score System score; LTE, optional long-term extension; OLE, open-label extension; qd, once daily.

Statistical Analyses

- Analyses of Week 52 endpoints were based on observed values without imputation for missing values

Results

Patients

- Of the 207 patients treated in the placebo-controlled period, 174 entered the OLE period (**Figure 2**, **Table 1**)
  - Overall, 53 (30.5%) patients discontinued treatment in the OLE, most commonly from withdrawal by patient (n=20, 11.5%), lost to follow-up (n=14, 8.0%), and adverse events (n=7, 4.0%)

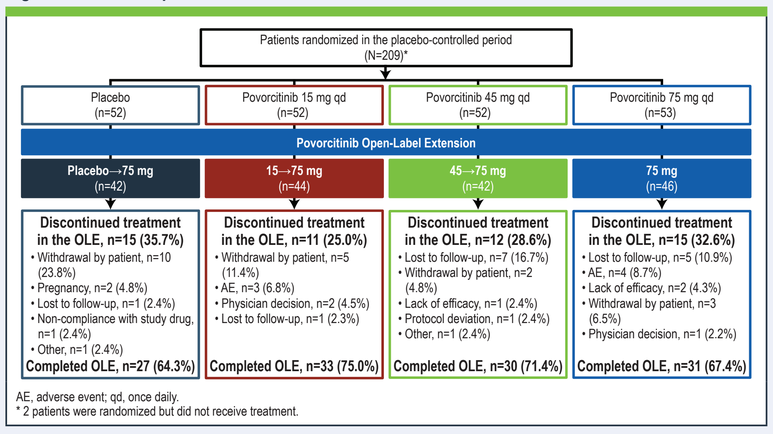
AN Count in the OLE Period

- Povorcitinib was associated with reduced AN counts from Day 1 baseline over time and low rates of HS flares in the OLE (**Figure 3**)
  - Mean (SD) change in AN count from Day 1 baseline at Week 52 was −5.7 (7.3), −8.4 (5.6), −10.4 (14.6), and −5.4 (5.6) in the placebo→75 mg, 15→75 mg, 45→75 mg, and 75 mg groups, respectively

HiSCR and IHS4 in the OLE Period

- Povorcitinib treatment was associated with improved HiSCR, HiSCR75, HiSCR90, and HiSCR100 rates over time in the OLE, especially in patients who switched from placebo to povorcitinib 75 mg qd (**Figure 4**)
- At Week 52, mean percentage change from Day 1 baseline in IHS4 in the placebo→75 mg, 15→75 mg, 45→75 mg, and 75 mg treatment groups was −52.8% (57.4), −67.7% (36.2), −72.5% (28.0), and −54.8% (49.5), respectively
- The percentage of patients achieving IHS4-55, IHS4-75, IHS4-90, and IHS4-100 improved in the OLE with povorcitinib 75 mg qd treatment (**Figure 5**)

Figure 2. Patient Disposition



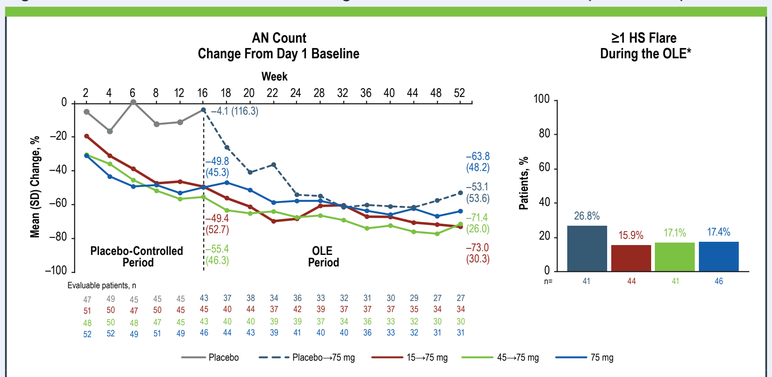
AE, adverse event; qd, once daily.
* 2 patients were randomized but did not receive treatment.

Table 1. Day 1 Baseline Demographic and Clinical Characteristics (OLE Population)

Characteristic	Total (N=174)	Placebo→75 mg (n=42)	15→75 mg (n=44)	45→75 mg (n=42)	75 mg (n=46)
Age, mean (SD), y	37.6 (11.2)	35.0 (9.8)	39.5 (10.8)	37.6 (12.7)	38.3 (11.0)
Women, n (%)	130 (74.7)	35 (83.3)	31 (70.5)	31 (73.8)	33 (71.7)
Race, n (%)					
White	120 (69.0)	31 (73.8)	32 (72.7)	26 (61.9)	31 (67.4)
Black/African American	44 (25.3)	9 (21.4)	9 (20.5)	12 (28.6)	14 (30.4)
Other	10 (5.7)	2 (4.8)	3 (6.8)	4 (9.5)	1 (2.2)
HS duration, mean (SD), y	10.5 (9.6)	7.9 (6.6)	10.2 (8.5)	11.3 (12.1)	12.6 (10.1)
BMI, mean (SD), kg/m^2	35.4 (8.6)	33.8 (8.7)	35.4 (7.4)	36.4 (10.2)	35.8 (7.9)
Current or former smoker, n (%)	99 (56.9)	20 (47.6)	28 (63.6)	26 (61.9)	25 (54.3)
Hurley stage, n (%)					
I	14 (8.0)	4 (9.5)	3 (6.8)	4 (9.5)	3 (6.5)
II	122 (70.1)	28 (66.7)	34 (77.3)	29 (69.0)	31 (67.4)
III	38 (21.8)	10 (23.8)	7 (15.9)	9 (21.4)	12 (26.1)
Previous biologic treatment, n (%)	35 (20.1)	6 (14.3)	8 (18.2)	13 (31.0)	8 (17.4)
AN count, mean (SD)	11.2 (8.3)	10.6 (5.3)	11.3 (6.1)	12.6 (12.5)	10.5 (7.5)
Draining tunnel count, mean (SD)	2.2 (3.8)	2.5 (3.9)	2.0 (4.0)	2.5 (4.4)	1.8 (3.0)
IHS4 score, mean (SD)	21.7 (19.6)	22.1 (16.1)	20.8 (20.0)	24.3 (23.7)	19.7 (18.3)

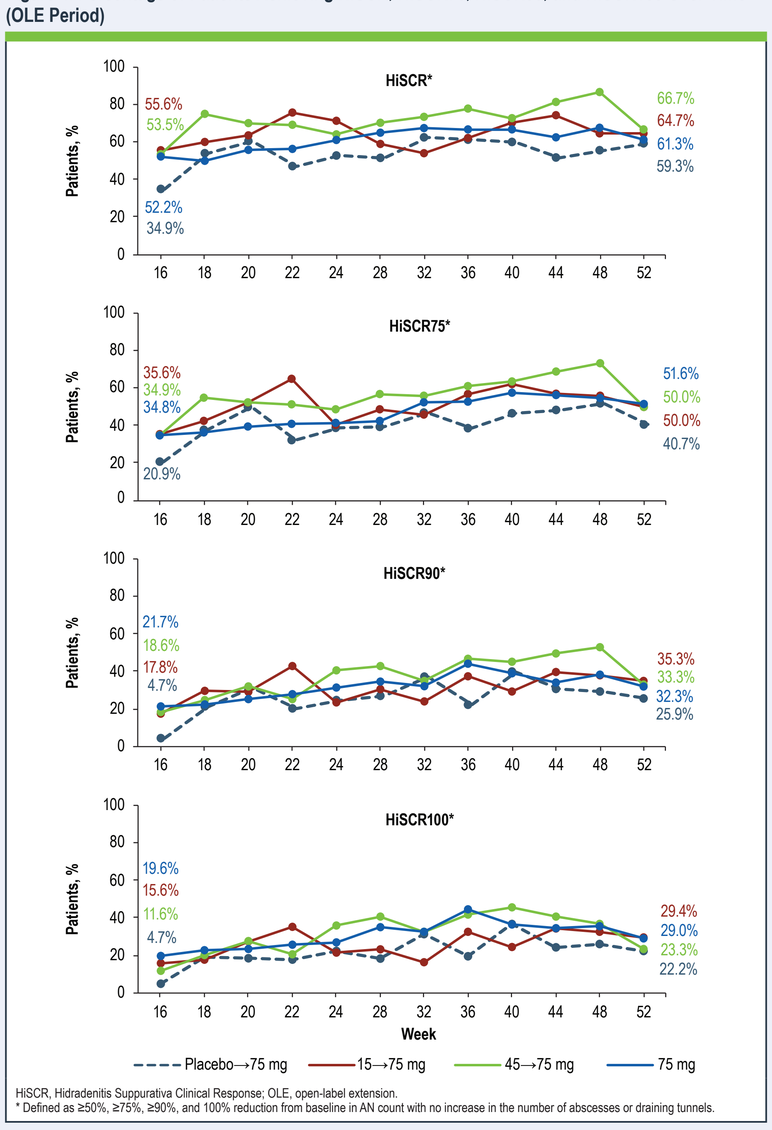
AN, abscess and inflammatory nodule; BMI, body mass index; HS, hidradenitis suppurativa; IHS4, International Hidradenitis Suppurativa Severity System Score; OLE, open-label extension.

Figure 3. AN Count Over Time and Percentage of Patients With ≥1 HS Flare (OLE Period)



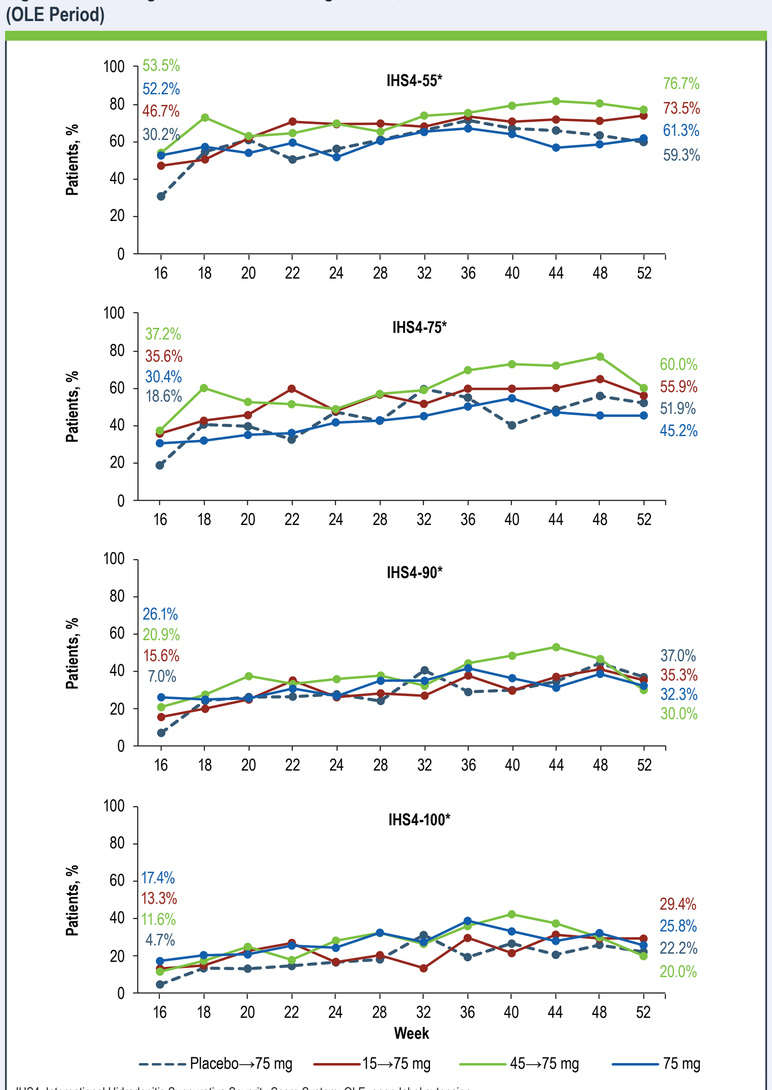
AN, abscess and inflammatory nodule; OLE, open-label extension.
* Defined as ≥25% increase from baseline in AN count with minimum increase of 2 AN.

Figure 4. Percentage of Patients Achieving HiSCR, HiSCR75, HiSCR90, and HiSCR100 Over Time (OLE Period)



HiSCR, Hidradenitis Suppurativa Clinical Response; OLE, open-label extension.
* Defined as ≥50%, ≥75%, ≥90%, and 100% reduction from baseline in AN count with no increase in the number of abscesses or draining tunnels.

Figure 5. Percentage of Patients Achieving IHS4-55, IHS4-75, IHS4-90, and IHS4-100 Over Time (OLE Period)



IHS4, International Hidradenitis Suppurativa Severity Score System; OLE, open-label extension.
* Defined as ≥55%, ≥75%, ≥90%, or 100% reduction from baseline in IHS4.

Safety

- Overall, 76.4% of patients experienced treatment-emergent adverse events (TEAEs) in the OLE period (**Table 2**); there were no fatal TEAEs

Table 2. Safety in the OLE Period

Patients,* n (%)	Total (N=174)	Placebo→75 mg (n=42)	15→75 mg (n=44)	45→75 mg (n=42)	75 mg (n=46)
TEAE	133 (76.4)	32 (76.2)	34 (77.3)	35 (83.3)	32 (69.6)
SAE	9 (5.2)	1 (2.4)	3 (6.8)	1 (2.4)	4 (8.7)
Grade ≥3 TEAE	15 (8.6)	2 (4.8)	3 (6.8)	3 (7.1)	7 (15.2)
TEAE leading to discontinuation	6 (3.4)	0	3 (6.8)	0	3 (6.5)
Most common TEAEs					
COVID-19	37 (21.3)	8 (19.0)	8 (18.2)	9 (21.4)	12 (26.1)
Acne	20 (11.5)	8 (19.0)	4 (9.1)	4 (9.5)	4 (8.7)
Upper respiratory tract infection	19 (10.9)	4 (9.5)	5 (11.4)	5 (11.9)	5 (10.9)
Headache	10 (5.7)	3 (7.1)	5 (11.4)	1 (2.4)	1 (2.2)
Nasopharyngitis	10 (5.7)	2 (4.8)	5 (11.4)	3 (7.1)	0
Urinary tract infection	10 (5.7)	4 (9.5)	1 (2.3)	3 (7.1)	2 (4.3)
Blood CK increased	9 (5.2)	2 (4.8)	3 (6.8)	3 (7.1)	1 (2.2)
Select TEAEs					
Platelet count decreased	5 (2.9)	2 (4.8)	1 (2.3)	1 (2.4)	1 (2.2)
Anemia	3 (1.7)	0	1 (2.3)	0	2 (4.3)
Herpes zoster	3 (1.7)	0	1 (2.3)	0	2 (4.3)

CK, creatine phosphokinase; OLE, open-label extension; SAE, serious adverse event; TEAE, treatment-emergent adverse event.
* Safety population included all patients who received ≥1 dose of the study drug during the OLE.

- Ten serious adverse events (SAEs) were reported in 9 patients, including myocardial infarction, congestive heart failure, infections (diverticulitis, perirectal abscess, sepsis), fall, diabetic ketoacidosis, ovarian cyst, pulmonary embolism, and HS
  - Congestive heart failure (45→75 mg); 59 y/o male, study Day 180 (OLE Day 61)
    - Risk factors included morbid obesity (body mass index [BMI] 65.4 kg/m^2), hypertension, coronary artery disease, hyperlipidemia, type 2 diabetes mellitus, stent (left anterior descending artery)
  - Myocardial infarction (75 mg); 42 y/o female, study Day 237 (OLE Day 148)
    - Risk factors included obesity (BMI 36.9 kg/m^2), high blood pressure, and hyperlipidemia
  - Pulmonary embolism (15→75 mg); 43 y/o male, study Day 167 (OLE Day 48)
    - Risk factors included obesity (BMI 38.4 kg/m^2), hypertension, active smoker, and bilateral knee sprains requiring immobilization for 1 month
- No SAEs in the OLE period were considered related to treatment by the investigator

Conclusions

- **Results from the OLE of this phase 2 trial show that average efficacy improved for all treatment arms following the switch to povorcitinib 75 mg qd**
- **Clinical improvements associated with povorcitinib 75 mg qd during the OLE were durable, with responses observed among the strictest outcomes**
  - **HiSCR100 was achieved by 22% to 29% of patients**
  - **IHS4-100 was achieved by 20% to 29% of patients**
- **Povorcitinib 75 mg qd continued to be generally well tolerated through 52 weeks of treatment**
- **Recruitment is open in the phase 3 INCB 54707-301 study of povorcitinib vs placebo in patients with moderate-to-severe HS**

Disclosures

JSK has served as a speaker for AbbVie, Janssen, Novartis, and UCB; and as a consultant for AbbVie, Bayer, ChemoCentryx, Incyte Corporation, InflaRx, Insmed, 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, Novartis, Boehringer Ingelheim, 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 abstract. 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, Almirall, Biogen 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, EvoImmune, Moonlake, Sonoma Bio, and Ventyx; receives fellowship funding from AbbVie and Janssen; and serves on the Board of Directors for Almirall.

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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