

Effects of the Janus Kinase 1 Inhibitor Povorcitinib (INCB054707) on Patient-Reported Skin Pain, Analgesic Use, and Itch in 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 scarring¹
- Pain and itch are among the most burdensome physical symptoms for patients with HS^{2,3}
 - Pain in HS is positively associated with disease severity^{3,4}
 - Itch and pain intensity are positively associated with quality-of-life impact in HS⁵
 - A substantial proportion of patients with HS resort to analgesics, including opioids, for management of their pain⁶ and are at increased risk of substance use disorder⁷
- Dysregulation of the Janus kinase (JAK)/signal transducer and activator of transcription (STAT) pathway is involved in a wide variety of inflammatory disorders, including HS⁸
 - Inhibition of the JAK pathway is associated with suppression of itch⁹
- 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 HS¹⁰; doses of 30 mg, 60 mg, and 90 mg were generally well tolerated, with no serious adverse events

Objective

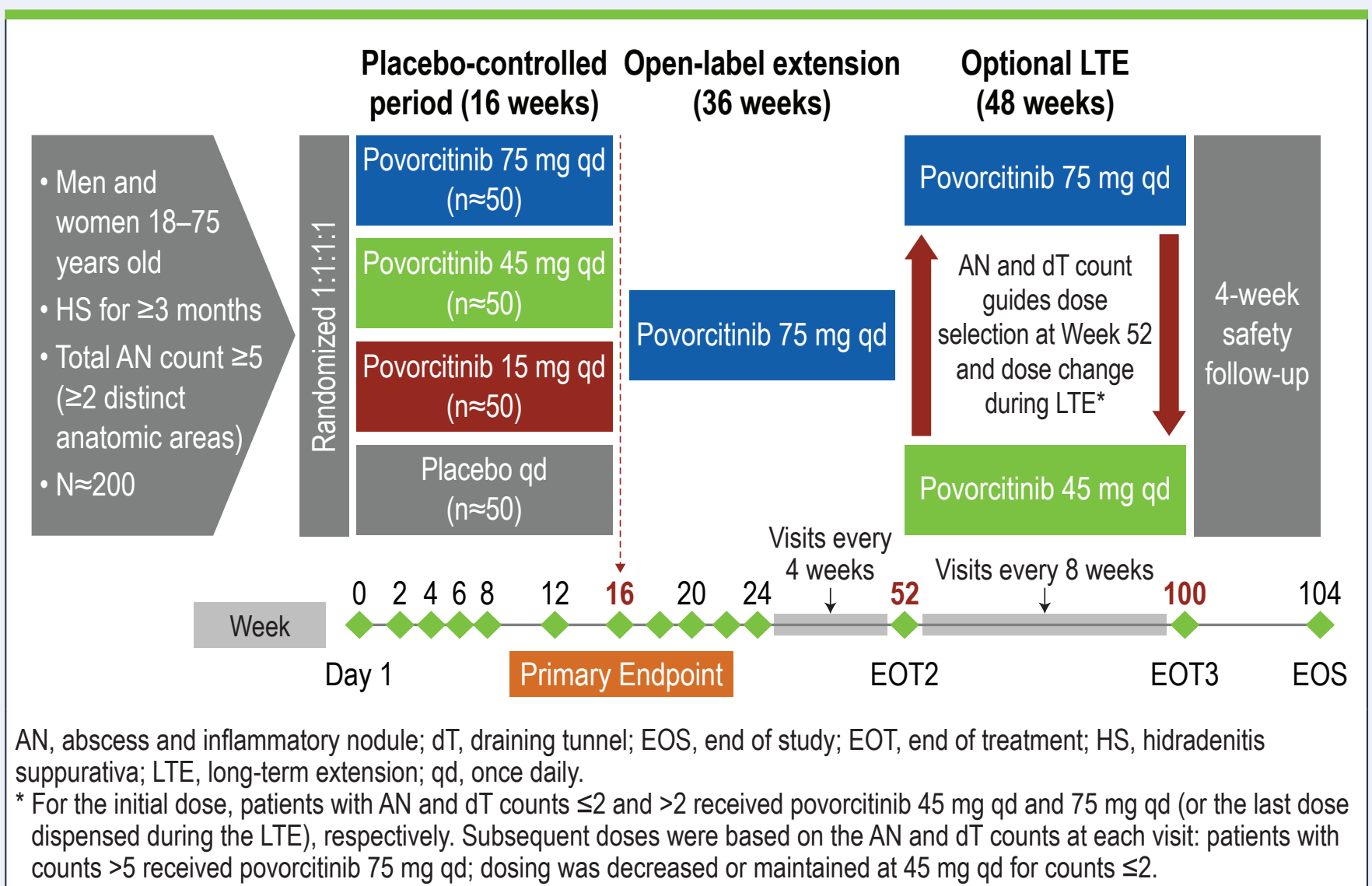
- To describe the effects of povorcitinib treatment on patient-reported skin pain, analgesic use, and itch over 16 weeks of treatment in adults with HS enrolled in a phase 2 dose-ranging study (NCT04476043; EudraCT 2020-001981-13)

Methods

Patients and Study Design

- Eligible patients were men and women aged 18–75 years, with HS (Hurley stage I, II, or III) of at least 3 months' duration at screening (**Figure 1**)
 - Diagnosis of HS was defined as total abscess and inflammatory nodule 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 $<3.0 \times 10^9/L$, absolute neutrophil count $<1.5 \times 10^9/L$, lymphocytes $<0.8 \times 10^9/L$, hemoglobin <9 g/dL, or platelet count $<150 \times 10^9/L$), had previously failed to respond to any JAK inhibitor, or had used immunomodulating biologic drugs within 12 weeks (or 5 half-lives)
- There were no eligibility criteria based on Skin Pain or Itch numerical rating scale (NRS) score at baseline; continued use of analgesics (opioid and nonopioid) with dose and treatment changes was permitted during the course of the study
- 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



Endpoints and Assessments

- Pain and itch were assessed daily via the Skin Pain NRS and Itch NRS, respectively
 - The NRS captures worst skin pain and itch on an 11-point scale, ranging from 0 (none) to 10 (worst imaginable), over a 24-hour recall period
 - Patients recorded pain, analgesic use (opioid and nonopioid), and itch via daily diary entries
- The following assessments were performed from Weeks 2 to 16:
 - Mean change from baseline in Skin Pain NRS
 - Mean change from baseline in Itch NRS
 - Percentage of patients achieving clinically meaningful reduction from baseline in Skin Pain NRS (defined as $\geq 30\%$ and ≥ 1 unit change from baseline; NRS30)
 - Percentage of patients achieving clinically meaningful reduction from baseline in Itch NRS (ie, ≥ 4 points)
 - Percentage of patients reporting analgesic use

Statistical Analysis

- All analyses are presented through 16 weeks of double-blind, placebo-controlled treatment
- All randomized patients were included in the intent-to-treat population, which was used for all patient-reported outcomes
- All patient-reported 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 typical for patients with HS¹¹
 - Median (range) age was 36 (19–70) years
 - Median (range) body mass index was 35.0 (19.8–66.6) kg/m²
 - 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
- 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
- Skin Pain and Itch NRS at baseline were generally balanced across groups
 - Mean (SD) baseline Skin Pain NRS score was 5.1 (2.6)
 - Mean (SD) baseline Itch NRS score was 4.5 (2.8)
- 26.8% (55/205) of patients reported baseline analgesic use for management of HS symptoms; 6.3% (13/205) reported baseline opioid use

Skin Pain

- Dose-dependent improvements from baseline in Skin Pain NRS were seen with povorcitinib as early as Week 2 and maintained through Week 16 (mean [SD] change at Week 16: 15 mg, -0.4 [2.4]; 45 mg, -1.4 [2.5]; 75 mg, -1.8 [2.5] vs -0.8 [2.1] for placebo; **Figure 2A**)
- Among patients with baseline Skin Pain NRS ≥ 1 treated with 15, 45, and 75 mg povorcitinib, 41.5%, 52.5%, and 53.7%, respectively, achieved Skin Pain NRS30 at Week 16 vs 31.4% for placebo (**Figure 2B**)

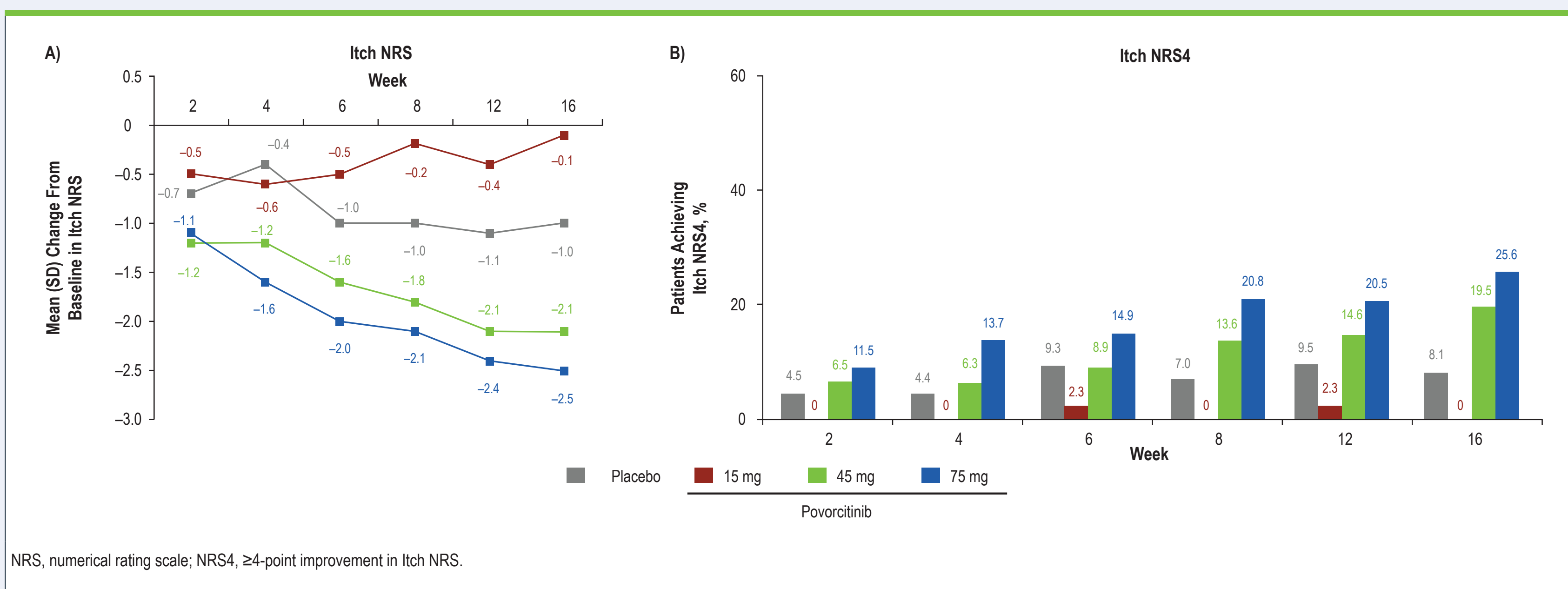
Itch

- Mean (SD) change from baseline in Itch NRS at Week 16 was -0.1 (1.7), -2.1 (2.3), and -2.5 (2.7) for 15, 45, and 75 mg povorcitinib, respectively, vs -1.0 (2.2) for placebo (**Figure 3A**)
- 19.5% and 25.6% of patients treated with 45 and 75 mg povorcitinib, respectively, achieved a ≥ 4 -point improvement in Itch NRS at Week 16 vs 8.1% for placebo (**Figure 3B**)

Analgesic Use

- 17.8%, 14.6%, and 9.1% of patients treated with 15, 45, and 75 mg povorcitinib, respectively, reported using analgesics at the time of the Week 16 study visit vs 16.2% for placebo
- The change from baseline in the percentage of patients reporting analgesic use at Week 16 with 15, 45, and 75 mg povorcitinib was -5.7% , -12.9% , and -23.6% , respectively, vs -7.3% for placebo (**Figure 4**)
- The percentages of patients reporting opioid use at the time of the Week 16 study visit were 4.4%, 4.9%, and 2.3% for 15, 45, and 75 mg povorcitinib, respectively, vs 8.1% for placebo

Figure 3. (A) Change From Baseline in Itch NRS and (B) Proportion of Patients Achieving Itch NRS4



NRS, numerical rating scale; NRS4, ≥ 4 -point improvement in Itch NRS.

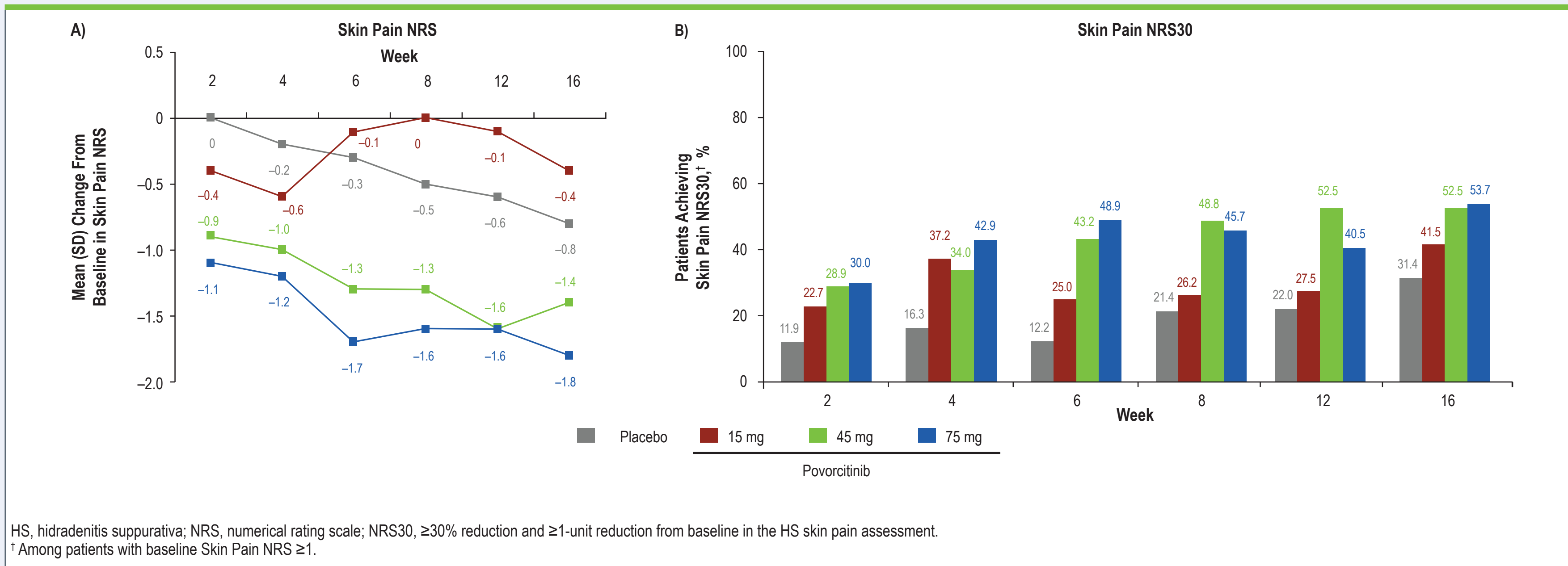
Table 1. Patient Demographics and Baseline Clinical Characteristics

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)
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)
Analgesic use, n/N (%)†					
Opioids	12/51 (23.5)	12/51 (23.5)	14/51 (27.5)	17/52 (32.7)	55/205 (26.8)
Skin Pain NRS, mean (SD)	5.4 (2.8)	4.6 (2.4)	5.1 (2.3)	5.2 (2.7)	5.1 (2.6)
Itch NRS, mean (SD)	4.8 (3.0)	3.7 (2.5)	4.8 (2.7)	5.0 (2.7)	4.5 (2.8)

BMI, body mass index; NRS, numerical rating scale.

* Includes one patient who identified as American Indian/Alaska native; † 4 patients did not provide data on analgesic use.

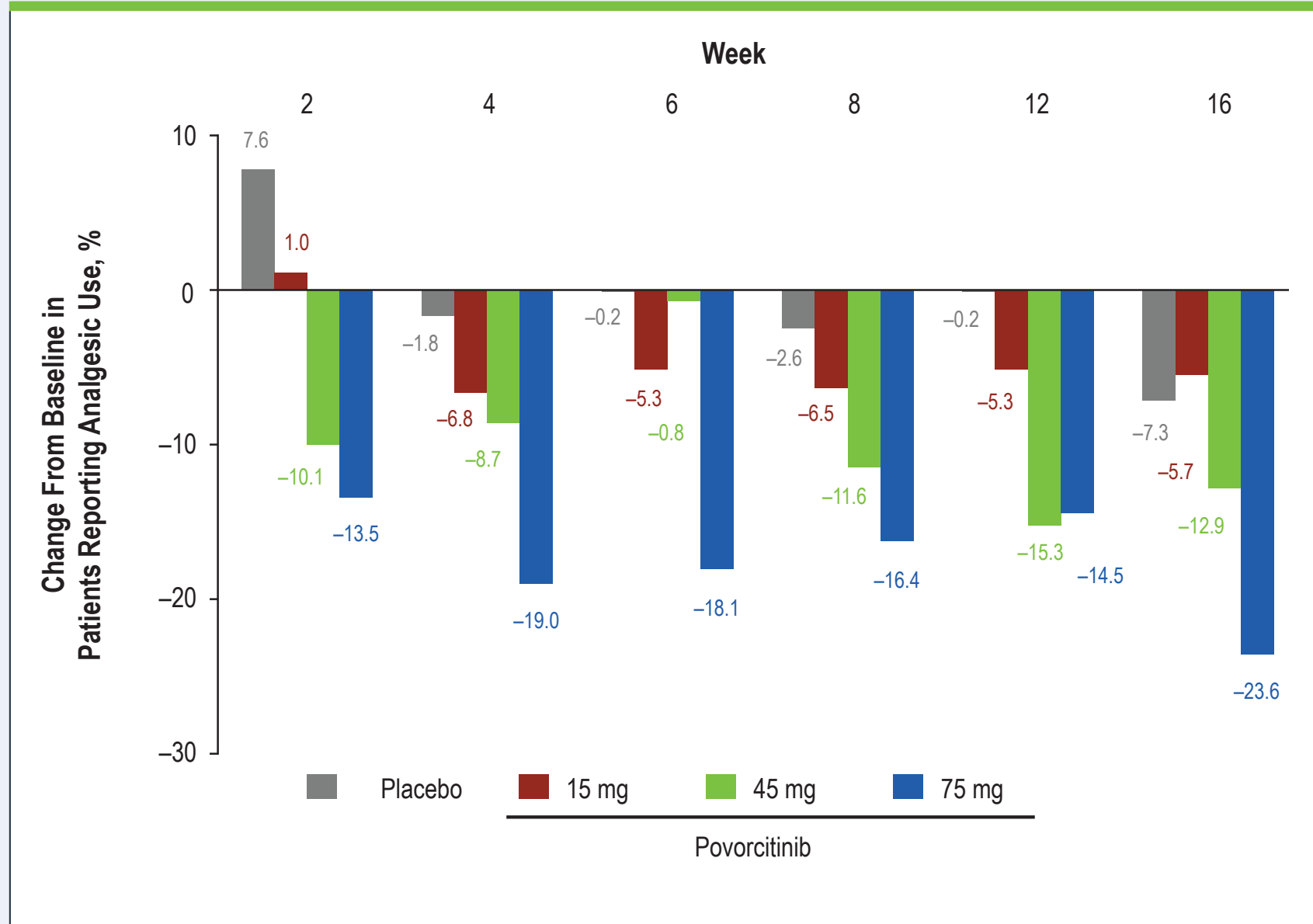
Figure 2. (A) Mean Change From Baseline in Skin Pain NRS and (B) Percentage of Patients Achieving Skin Pain NRS30



HS, hidradenitis suppurativa; NRS, numerical rating scale; NRS30, $\geq 30\%$ reduction and ≥ 1 -unit reduction from baseline in the HS skin pain assessment.

† Among patients with baseline Skin Pain NRS ≥ 1 .

Figure 4. Change From Baseline in Percentage of Patients Reporting Analgesic Use



Conclusions

- Results from this phase 2 study of povorcitinib in patients with HS suggest that patient-reported skin pain and itch were dose-dependently improved with povorcitinib treatment in patients with HS**
- Frequency of analgesic use, including overall analgesic use and opioid use, trended downward across all treatment arms, but with a more pronounced effect in patients receiving 75 mg**
- 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 Corporation, 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. KBrown, LLS, AW, and KBibeau 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, Evolmmune, 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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