3000368

Presented at the
Ninth Annual Symposium on Hidradenitis Suppurativa Advances (SHSA)
Austin, TX, USA • November 1–3, 2024

Safety of Povorcitinib During 84 Weeks of Treatment: Post Hoc Analysis of a Phase 2 HS Study

Christopher J. Sayed, MD,[1] Falk G. Bechara, MD,[2] Christos C. Zouboulis, MD, PhD,[3] Martin M. Okun, MD, PhD,[4] Susan Poelman, MSc, MD, FRCPC,[5] Jacek C. Szepietowski, MD, PhD, FRCP (Edin),[6] Alexa B. Kimball, MD,[7] Joslyn S. Kirby, MD, MS, MEd,[8] Leandro L. Santos, MS,[8] Zhenyi Xue, PhD,[8] Martina L. Porter, MD[7]

[1]Department of Dermatology, University of North Carolina School of Medicine, Chapel Hill, NC, USA; [2]ICH—International Center for Hidradenitis Suppurativa/Acne Inversa, Department of Dermatology, Ruhr-University, Bochum, Germany; [3]Staedtisches Klinikum Dessau, Brandenburg Medical School Theodor Fontane and Faculty of Health Sciences Brandenburg, Dessau, Germany; [4]Fort Memorial Hospital, Fort Atkinson, WI, USA; [5]Beacon Dermatology, Calgary, AB, Canada; [6]Department of Dermatology, Venereology and Allergology, Wroclaw Medical University, Wroclaw, Poland; [7]Harvard Medical School and Beth Israel Deaconess Medical Center, Boston, MA, USA; [8]Incyte Corporation, Wilmington, DE, USA

Plain Language Summary

- **Why was this study needed?:** Effective treatments for patients with hidradenitis suppurativa (HS) will require long-term use, and safety of new treatments is a concern for physicians and patients
- **What did this study show?:** Povorcitinib, a selective JAK1 inhibitor in clinical studies to treat HS, was associated with infrequent and generally mild adverse events with daily oral administration for nearly 2 years
- **Why this is important:** All treatments for HS should be taken with their potential risks and benefits in mind. Our study provides patients and clinicians with more information about the safety of povorcitinib with long-term treatment

Introduction

- Povorcitinib is an oral, selective Janus kinase (JAK)1 inhibitor with demonstrated efficacy in a phase 2 clinical trial for HS[1,2]

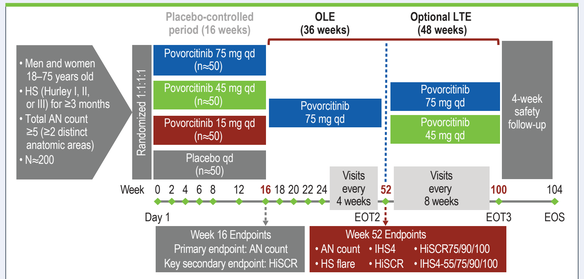
Objective

- To determine the frequency and severity of select adverse events (AEs) and potentially clinically important laboratory parameters over 84 weeks of treatment

Methods

- This is a post hoc analysis of a phase 2 randomized clinical study
- After a 16-week placebo-controlled period, patients entered a 36-week open-label extension (OLE) to receive once-daily (qd) povorcitinib 75 mg, followed by a 48-week long-term extension (LTE; povorcitinib 45 or 75 mg qd; **Figure 1**)
- The safety database was searched for relevant MedDRA terms
- Potentially clinically important laboratory parameters were identified based on their CTCAE grading, upper limits of normal, or change from baseline

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



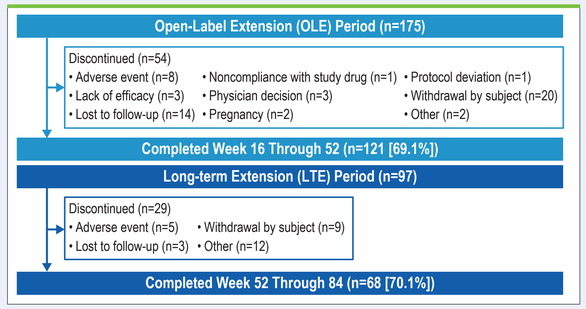
AN, abscess and inflammatory nodule; EOS, end of study; EOT, end of treatment; HiSCR, ≥50% reduction from baseline in AN count with no increase in the number of abscesses or draining tunnels (Hidradenitis Suppurativa Clinical Response); HiSCR75/90/100, ≥75%/90%/100% reduction from baseline in AN count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

Results

Patient Disposition

- 175 patients entered the OLE, and 97 entered the LTE **(Figure 2)**

Figure 2. Patient Disposition During the OLE and LTE Periods



Safety

- The most common AEs in the combined OLE and LTE were COVID-19 (29.1%), upper respiratory tract infection (13.1%), acne (12.6%), nasopharyngitis (8.0%), blood creatine phosphokinase (CPK) increased (6.9%), urinary tract infection (6.9%), headache (5.7%), and worsening of HS (5.7%; **Table 1**)

Table 1. Safety Summary During the OLE and LTE

Event, n (%)	OLE + LTE (N=175)	OLE (n=175)	LTE (n=97)
Patients with TEAE	144 (82.3)	135 (77.1)	64 (66.0)
Most common TEAEs*			
COVID-19	51 (29.1)	36 (20.6)	18 (18.6)
Acne	22 (12.6)	20 (11.4)	3 (3.1)
Upper respiratory tract infection	23 (13.1)	19 (10.9)	7 (7.2)
Headache	10 (5.7)	10 (5.7)	1 (1.0)
Nasopharyngitis	14 (8.0)	10 (5.7)	6 (6.2)
Urinary tract infection	12 (6.9)	10 (5.7)	2 (2.1)
Blood CPK increased	12 (6.9)	9 (5.1)	3 (3.1)
Hidradenitis	10 (5.7)	6 (3.4)	4 (4.1)
Fatigue	9 (5.1)	8 (4.6)	1 (1.0)
Sinusitis	9 (5.1)	5 (2.9)	4 (4.1)
Patients with treatment-related TEAE	54 (30.9)	43 (24.6)	17 (17.5)
Patients with serious TEAE	14 (8.0)	9 (5.1)	5 (5.2)
Patients with grade ≥3 TEAE	21 (12.0)	15 (8.6)	6 (6.2)
Patients with TEAE leading to dose interruption	34 (19.4)	26 (14.9)	11 (11.3)
Patients with TEAE leading to discontinuation†	10 (5.7)	6 (3.4)	4 (4.1)

CPK, creatine phosphokinase; LTE, long-term extension; OLE, open-label extension; TEAE, treatment-emergent adverse event.
* Occurring in ≥5% of patients in the OLE+LTE population. † TEAEs leading to dose discontinuation were anemia (n=2), acute myocardial infarction, folliculitis, increased blood CPK, pulmonary embolism, worsening hidradenitis, gastrointestinal hemorrhage, breast abscess, and lung adenocarcinoma.

- Serious AEs (SAEs) and grade ≥3 AEs were reported in 14 (8.0%) and 21 (12.0%) patients, respectively
  - There were 4 SAEs relevant to the JAK inhibitor class, one pulmonary embolism, one myocardial infarction (MI), and 2 malignancies **(Table 2)**
  - All SAEs were deemed to have alternate causality, and none were considered treatment related
- Dose interruptions occurred in 34 (19.4%) patients, and 10 (5.7%) discontinued due to an AE

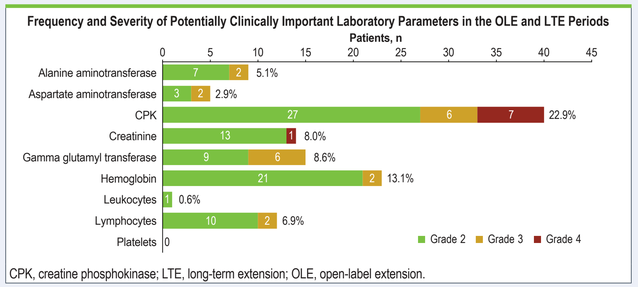
Table 2. Brief Patient Narratives for SAEs Relevant to the JAK Inhibitor Class

Patient	Narrative
1	A 33-year-old white male was newly diagnosed with metastatic (stage 4) lung adenocarcinoma. He was a current and long-time tobacco user. He was withdrawn from the study and began chemotherapy soon after.
2	A 43-year-old Black male experienced a pulmonary embolism. He had a medical history of hypertension, obesity, had been immobilized for months prior to the event due to bilateral knee sprains, and was also found to be COVID positive.
3	A 41-year-old Black female was diagnosed with an acute myocardial infarction. She had a history of obesity and used tobacco.
4	A 43-year-old Black female was newly diagnosed with metastatic (stage 4) breast cancer during the safety follow-up period. She had a medical history of type 2 diabetes and hypertension. She died approximately 30 days later.
For each of these events, the investigator assessed that there is not a reasonable possibility that povorcitinib caused this TEAE.	

JAK, Janus kinase; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

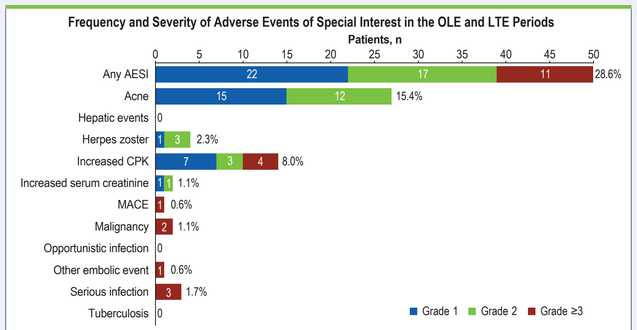
- Potentially clinically important laboratory parameters were infrequent and generally grade 1 or 2 **(Figure 3)**
  - Hemoglobin <8.0 g/dL occurred in 2 (1.1%) patients
  - The proportion of patients with total, HDL, and LDL cholesterol >1.5× from baseline were 3.4%, 6.9%, and 10.9%, respectively, in the combined OLE and LTE
- Few malignancies, major cardiovascular events, or deep venous thromboses were reported **(Figure 4)**

Figure 3. Potentially Clinically Important Laboratory Parameters



CPK, creatine phosphokinase; LTE, long-term extension; OLE, open-label extension.

Figure 4. Adverse Events of Special Interest



AESI, adverse event of special interest; CPK, creatine phosphokinase; LTE, long-term extension; MACE, major adverse cardiovascular event; OLE, open-label extension.
* Serious infections included sepsis, worsening of diverticulitis, and perirectal abscess, all of which resolved.

Conclusions

- **In this phase 2 study, long-term treatment with oral povorcitinib demonstrated a safety profile consistent with the class of JAK1 inhibitors**
- **Povorcitinib was generally well tolerated with no new safety concerns identified**
- **Adverse events of special interest and potentially clinically important laboratory parameters over the study period were infrequent and generally mild (grade 1 or 2) in severity**
  - **No cases of tuberculosis or opportunistic infections were observed**
- **Two phase 3 studies of povorcitinib in patients with moderate to severe HS are in progress and will provide additional data on efficacy and safety in a larger group of patients**

Disclosures

CJS acted as an investigator for AbbVie, AstraZeneca, Chemocentryx, GSK, Incyte, InflaRx, Novartis, and UCB Pharma; reports consultancy fees from AbbVie, Alumis, AstraZeneca, InflaRx, Incyte, Logical Images, Sonoma Biotherapeutics, and UCB Pharma; and acted as a speaker for AbbVie and Novartis. **FGB** has received honoraria for participation in advisory boards, in clinical trials, and/or as a speaker from AbbVie, AbbVie Deutschland, Acelyrin, Boehringer Ingelheim, Celltrion, Dr. Wolff, Incyte, Janssen-Cilag, Mölnlycke, MoonLake, Novartis, Sanofi, Sitala, and UCB. **CCZ** reports consultancy/advisory board disease-relevant honoraria from Boehringer Ingelheim, Eli Lilly, Idorsia, Incyte, Novartis, Pfizer, Sanofi, and UCB. He has received speaker fees from Novartis 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. **MMO** is a consultant for AbbVie, Azora, Bluefin, Boehringer Ingelheim, ChemoCentryx, Incyte, InflaRx, Innovaderm, Novartis, Pfizer, and Vyne. **SP** has served as a speaker for AbbVie, Janssen, Novartis, and UCB; and a consultant and/or investigator for AbbVie, Incyte, Janssen, MoonLake, Novartis, Pfizer, and UCB. **JCS** has served as an advisor for AbbVie, LEO Pharma, Novartis, Sanofi-Genzyme, Trevi, and UCB; has received speaker honoraria from AbbVie, Eli Lilly, Janssen-Cilag, LEO Pharma, Novartis, Sanofi-Genzyme, and Pfizer; and has received clinical trial funding from AbbVie, Almirall, Amgen, Galapagos, Holm, Incyte, InflaRx, Janssen-Cilag, Menlo Therapeutics, Merck, Novartis, Pfizer, Regeneron, Trevi, and UCB. **ABK's** institution received grants from AbbVie, Admirx, AnaptysBio, Aristea, Bristol Myers Squibb, Eli Lilly, Incyte, Janssen, MoonLake, Novartis, Pfizer, Prometheus, Sonoma Bio, and UCB; and fellowship funding from AbbVie and Janssen. She received consulting fees from AbbVie, Alumis, Bayer, Boehringer Ingelheim, Eli Lilly, Evommune, Janssen, MoonLake, Novartis, Pfizer, Priovant, Sanofi, Sonoma Bio, Target RWE, and UCB; and serves on the board of directors of Almirall. **JSK** is an employee and shareholder of Incyte Corporation; has served as a speaker for AbbVie; and as a consultant for AbbVie, Bayer, ChemoCentryx, InflaRx, Janssen, Novartis, Pfizer, and UCB. **LLS** and **ZX** are employees and shareholders of Incyte. **MLP** reports that her institution received grants from AbbVie, Admirx, Anaptys Bio, Acelyrin, Aristea, Avalo Therapeutics, Bayer, Bristol Myers Squibb, Lilly, Incyte, Insomed, Janssen, Moonlake, Novartis, Pfizer, Prometheus, Regeneron, Sanofi, Prometheus Labs, Oasis Pharmaceuticals, UCB and Sonoma Bio; she received consulting fees from Alumis, Avalo Therapeutics, FIDE, Incyte, Janssen, Trifecta Clinical/WCG, Moonlake, Novartis, Pfizer, Prometheus, Sonoma Bio, Sanofi, and UCB.

Acknowledgments

The authors wish to thank the patients and their families, the investigators, and the site personnel who participated in this study. This study was sponsored by Incyte Corporation (Wilmington, DE). Editorial assistance was provided by Nestor Davila, PhD, of ICON (Blue Bell, PA, USA), and was funded by Incyte.

References

1. Alavi A, et al. *Br J Dermatol.* 2022;186(5):803-813.
2. Kirby JS, et al. 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. Presented at: 31st Annual European Academy of Dermatology and Venereology Congress (EADV); September 7-10, 2022; Milan, Italy and online.

To download a copy of this poster, scan code