Efficacy, safety, and mechanism of action of abrocitinib in the treatment of prurigo nodularis and chronic pruritus of unknown origin

Shawn Kwatra*1, Zachary Bordeaux1,2, Thomas Pritchard1, Hannah Cornman1, Alexander Kollhoff1, Ahmad Rajeh3, Emily MA1, Jaya Manjunath1, Brenda Imo1, Kevin Lee1, Aaron Bao1, Anusha Kambala1, Varsha Parthasarathy1, Sriya Reddy1,2, Ali Alajmi1, Jingyi Zhang1, Junwen Deng1, Carly Dillen1, Madan Kwatra2

1Johns Hopkins University School of Medicine, Department of Dermatology, Baltimore, Maryland, United States, 2Duke University School of Medicine, Department of Anesthesiology, Durham, North Carolina, United States, 3Massachusetts General Hospital, Department of Dermatology, Boston, Massachusetts, United States

Introduction & Objectives: Prurigo nodularis (PN) and chronic pruritus of unknown origin (CPUO) are chronic pruritic diseases that dramatically impair quality of life, but therapeutic options are limited. Abrocitinib, a Janus kinase 1 (JAK1) inhibitor, represents a promising therapy for both conditions. Our objective was to assess the efficacy, safety, and transcriptomic effects of abrocitinib in the treatment of PN and CPUO.

Materials & Methods: We conducted a 12-week**, open-label, phase 2** trial of abrocitinib administered orally at 200 mg daily. Ten patients had moderate-to-severe PN (Peak Pruritus Numeric Rating Scale [PP-NRS] score ≥7 and Investigator Global Assessment [IGA] score ≥3) and 10 had moderate-to-severe CPUO (PP-NRS score ≥7). The primary efficacy endpoint was percent change in PP-NRS score from baseline to week 12. Secondary endpoints included percentage of patients achieving a ≥4-point reduction on the PP-NRS; percent change in Dermatology Life Quality Index (DLQI) score; and, for PN, percent change in IGA score. Cutaneous transcriptome analysis was performed at baseline and week 12.

Results: Mean baseline PP-NRS score was 9.2 for PN and 8.2 for CPUO. PP-NRS scores decreased by 78.3% in PN (p<0.001) and 53.7% in CPUO (p=0.01) by week 12. 80% of PN patients and 60% of CPUO patients achieved a ≥4-point decrease on the PP-NRS; percent change in Dermatology Life Quality Index (DLQI) score; and, for PN, percent change in IGA score. Cutaneous transcriptome analysis was performed at baseline and week 12.

Conclusion: Abrocitinib resulted in rapid and significant reduction of itch and disease severity in both PN and CPUO, with significant improvement in the molecular skin signature.