Examining the Relationships Among Abrocitinib Treatment, Itch, Skin Pain, and Work and Activity Impairments in Patients With Atopic Dermatitis: A Mediation Modeling Analysis

Jonathan I. Silverberg,[1] Sonja Ständer,[2] Jacob P. Thyssen,[3] Brian S. Kim,[4] Carla Castro,[5] Anthony Bewley,[6] Laurent Misery,[7] Andrew G. Bushmakin,[8] Joseph C. Cappelleri,[8] Erman Guler,[9] Justine Alderfer,[10] Melisa Watkins,[11] Gary Chan,[8] Daniela E. Myers[10]

[1]The George Washington University School of Medicine and Health Sciences, Washington, DC, USA; [2]Center for Chronic Pruritus, Münster University Hospital, Münster, Germany; [3]Bispebjerg Hospital, University of Copenhagen, Copenhagen, Denmark; [4]Precision Immunology Institute, Icahn School of Medicine at Mount Sinai, New York, NY, USA; [5]Hospital Universitario Austral and Universidad Austral, Pilar, Argentina; [6]Barts Health NHS Trust, London, United Kingdom; [7]University Hospital of Brest, Brest, France; [8]Pfizer Inc., Groton, CT, USA; [9]Pfizer Inc., Istanbul, Turkey; [10]Pfizer Inc., Collegeville, PA, USA; [11]Pfizer Inc., New York, NY, USA

Background: Atopic dermatitis (AD) is a chronic inflammatory skin disorder characterized by intense itch, skin pain, and impaired quality of life. Skin pain is a common and bothersome symptom of AD and increases in prevalence and intensity with worsening disease severity. Abrocitinib is an oral, once-daily, selective Janus kinase-1 inhibitor approved for the treatment of moderate-to-severe AD. Abrocitinib treatment resulted in improvements in skin clearance as well as rapid itch reduction in patients with moderate-to-severe AD across multiple phase 3 studies. Work productivity loss and activity impairment was assessed in the phase 3 JADE MONO-2 (NCT03575871) trial, with greater improvements being associated with abrocitinib treatment compared with placebo. The mechanism(s) through which abrocitinib reduces work productivity loss and activity impairment are unclear.

Objective: To describe the interrelationships among abrocitinib treatment, itch, skin pain, and work productivity and activity impairment using a mediation modeling analysis in patients with AD.

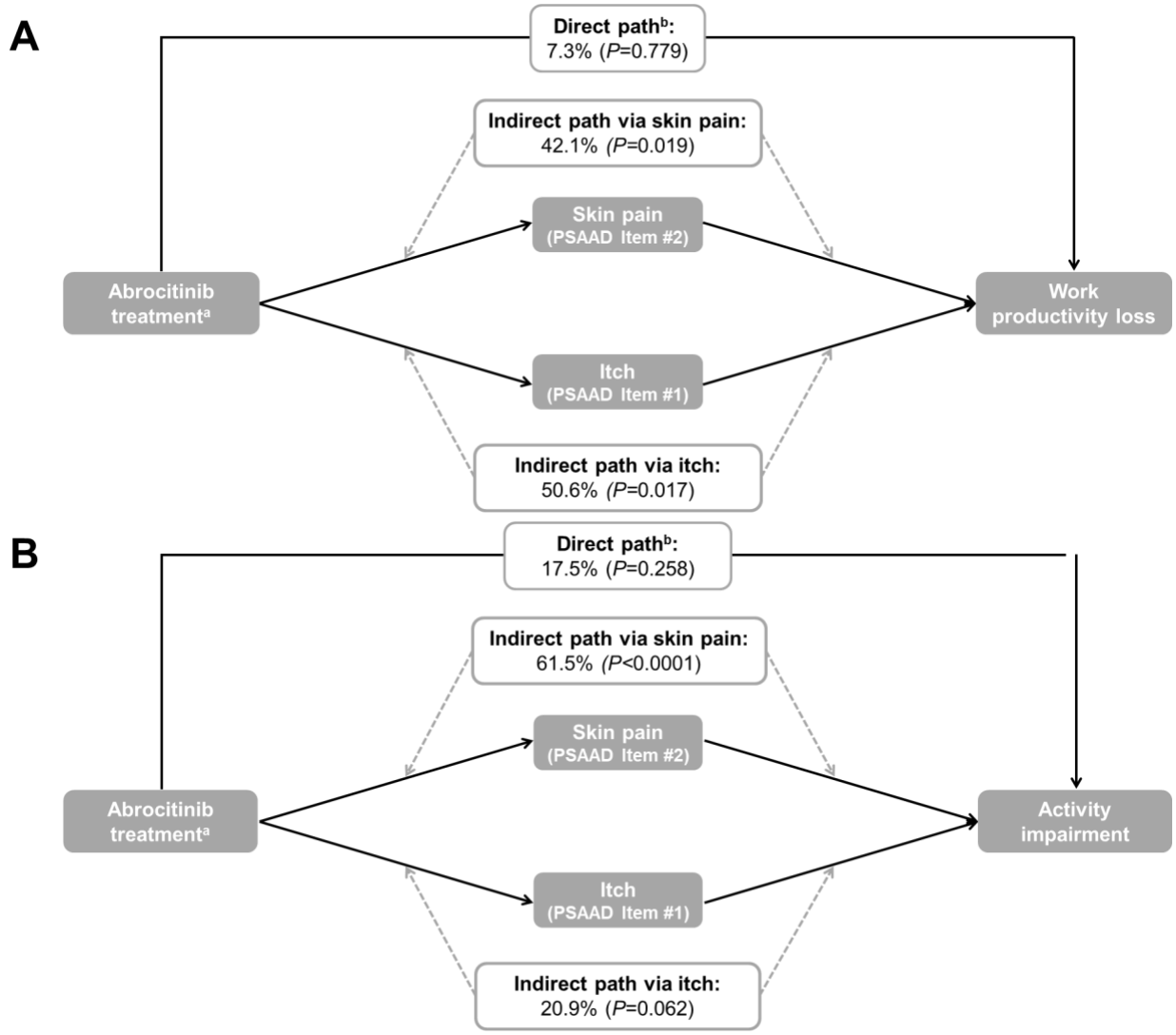
Methods: Data from adult patients treated with abrocitinib monotherapy (200 mg or 100 mg) or placebo in JADE MONO-2 were included in this analysis. As separate outcomes, work productivity loss and activity impairment (outcome variables) were measured by the Work Productivity and Activity Impairment Questionnaire: Atopic Dermatitis version 2.0 (WPAI-AD 2.0). Itch and skin pain (mediator variables) were evaluated using the Pruritus and Symptoms Assessment for Atopic Dermatitis (PSAAD) item #1 (*How itchy was your skin over the past 24 hours?*) and item #2 (*How painful was your skin over the past 24 hours?*), respectively. Mediation modeling was conducted independently for work productivity loss and activity impairment. All available data at week 12 were used in the modeling. Effects with $P<0.05$ were considered statistically significant.

Results: The direct effects of abrocitinib were estimated to be 7.3% ($P=0.779$) and 17.5% ($P=0.258$) on work productivity loss and activity impairment, respectively (**Figure 1A** and **1B**). The indirect effects of abrocitinib treatment on work productivity loss and, separately, on activity impairment mediated via itch were estimated to be 50.6% ($P=0.017$) and 20.9% ($P=0.062$), respectively, and via skin pain were estimated to be 42.1% and 61.5%, respectively ($P<0.05$ for both; **Figure 1A** and **1B**).

Conclusions: The indirect effect of abrocitinib treatment on work productivity loss is mediated approximately equally through the reduction in itch severity and skin pain. The effect of abrocitinib treatment on activity impairment is mostly mediated indirectly through the reduction of skin pain, along with a smaller indirect contribution from the reduction in itch. These findings support further research into the extent that patients consider itch and skin pain as separate concepts in terms of their impact on work productivity.

Keywords: abrocitinib, atopic dermatitis, skin pain, itch, work productivity.

Figure 1. Direct and indirect effects of abrocitinib treatment on (**A**) work productivity loss and (**B**) activity impairment in patients with atopic dermatitis.



PSAAD, Pruritus and Symptoms Assessment for Atopic Dermatitis.

[a]Abrocitinib treatment is a binary variable representing abrocitinib versus placebo.

[b]Direct path represents the effects of other factors not included in the model.

Acknowledgments: This study was sponsored by Pfizer. Editorial/medical writing support under the guidance of the authors was provided by Megan K. Elder, PhD, at ApotheCom, San

Francisco, CA, USA, and was funded by Pfizer Inc., New York, NY, USA, in accordance with Good Publication Practice (GPP 2022) guidelines (*Ann Intern Med*. 2022;10.7326/M22-1460).

Disclosures: Jonathan I. Silverberg has served as an investigator for Celgene, Eli Lilly, F. Hoffmann-LaRoche, Menlo Therapeutics, Realm Therapeutics, Regeneron, and Sanofi-Genzyme; as a consultant for Pfizer Inc., AbbVie, Anacor, AnaptysBio, Arena Pharmaceuticals, Dermavant, Dermira, Eli Lilly and Company, Galderma, GlaxoSmithKline, Glenmark, Incyte, Kiniksa Pharmaceuticals, LEO Pharma, Menlo Therapeutics, Novartis, Realm Therapeutics, Regeneron, and Sanofi-Genzyme; and as a speaker for Regeneron and Sanofi-Genzyme. **Sonja Ständer** is an investigator for Dermasence, Galderma, Kiniksa, Menlo Therapeutics, Novartis, Trevi Therapeutics, Sanofi-Genzyme, and Vanda; and a member of scientific advisory boards, consultant, and/or speaker for Pfizer Inc., AbbVie, Almirall, Beiersdorf, Bellus Health, Benevolent, Bionorica, Cara, Clexio, Eli Lilly and Company, Escient, Galderma, Grünenthal, Kiniksa, LEO Pharma, Menlo Therapeutics, P.G. Unna Academy, Sanofi-Genzyme, Trevi Therapeutics, and Vifor. **Jacob P. Thyssen** is an advisor for Pfizer Inc., AbbVie, Almirall, Arena Pharmaceuticals, Aslan Pharmaceuticals, Coloplast, Eli Lilly and Company, LEO Pharma, OM Pharma, Regeneron, Sanofi-Genzyme, and Union Therapeutics; a speaker for Pfizer Inc., AbbVie, Almirall, Eli Lilly and Company, LEO Pharma, Regeneron, and Sanofi Genzyme; and has received research grants from Pfizer Inc., Regeneron, and Sanofi Genzyme. **Brian S. Kim** is a consultant and advisor for Pfizer Inc., AbbVie, Boehringer Ingelheim, Cara Therapeutics, Kiniksa, Menlo Therapeutics, and Sanofi-Regeneron; has received research grants from Cara Therapeutics, Celgene, and LEO Pharma; and is founder and stockholder in Nuogen Pharma. **Carla Castro** has served as an investigator for Pfizer Inc., AbbVie, Eli Lilly and Company, La Roche Posay, Novartis, and Sanofi; and an advisor for Pfizer Inc., AbbVie, CeraVe, Eli Lilly and Company, Janssen, Novartis, and Sanofi; and speaker for Pfizer Inc., AbbVie, CeraVe, Eli Lilly and Company, Eucerin, Galderma, ISDIN, Janssen, La Roche Posay, Novartis, and Sanofi; and

has received grants for investigation from Pfizer Inc. **Anthony Bewley** has acted as a consultant for and has received travel grants from AbbVie, Almirall, Eli Lilly and Company, Galderma, Janssen, LEO Pharma, Novartis, Sanofi-Genzyme, and UCB. **Laurent Misery** has acted as an investigator for Pfizer Inc., AbbVie, Eli Lilly and Company, Galderma, Kiniksa, Menlo Therapeutics, Novartis, Sanofi-Genzyme, and Trevi Therapeutics; and a consultant for AbbVie, Beiersdorf, Clexio, Eli Lilly and Company, Galderma, LEO Pharma, Menlo Therapeutics, Novartis, Sanofi Genzyme, Sienna Biopharmaceuticals, and Trevi Therapeutics. **Andrew G. Bushmakin**, **Joseph C. Cappelleri**, **Erman Guler**, **Justine Alderfer**, **Melissa Watkins**, **Gary Chan,** and **Daniela E. Myers** are employees and stock and/or shareholders of Pfizer Inc.