Examining the Relationships Among Abrocitinib Treatment, Itch, Skin Pain, and Dermatology-Specific Quality of Life in Patients with Atopic Dermatitis: A Mediation Modeling Analysis

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- **SS** 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.
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Introduction and Objective

Introduction

- Skin pain in AD is associated with a substantial health burden, similar to that of itch, and is known to contribute to sleep disruption and mood disturbance[1-3]
- Abrocitinib is an oral, once-daily, JAK1-selective inhibitor approved for the treatment of moderate-to-severe AD[4-7]
- In the phase 3 clinical trials JADE MONO-1 (NCT03349060) and JADE MONO-2 (NCT03575871), abrocitinib demonstrated rapid relief from itch and skin pain as well as meaningful improvements in QoL compared with placebo[8-10]
- The interrelationships among abrocitinib treatment and improvements in itch severity, skin pain, and QoL have not yet been investigated

Objective

- To characterize the effect of abrocitinib treatment via itch and skin pain on dermatology-related QoL in patients with AD using mediation modeling

AD, atopic dermatitis; JAK1, Janus kinase 1; QoL, quality of life.

1. Silverberg JI et al. *Ann Allergy Asthma Immunol.* 2018;121:340-347. 2. Silverberg JI et al. *J Allergy Clin Immunol Pract.* 2019;7:2699-2706. 3. Vakharia PP et al. *Ann Allergy Asthma Immunol.* 2017;119:548-552. 4. Cibinqo (abrocitinib), 100 mg film-coated tablets. Summary of product characteristics. Pfizer Ltd.; September 2021. 5. Cibinqo (abrocitinib) tablets, for oral use 50 mg 100 mg 200 mg. Summary of product characteristics. Pfizer Japan; 2021. 6. Cibinqo (abrocitinib). Summary of product characteristics. European Medicines Agency; December 2021. 7. Cibinqo (abrocitinib) tablets. Prescribing information. Pfizer Labs; January 2022.. 8 Simpson EL et al. *Lancet.* 2020;396:255-266. 9. Silverberg JI et al. *JAMA Dermatol.* 2020;156:863-873. 10.Gooderham MJ et al. *J Am Acad Dermatol.* 2022;87(Supplement):AB120.

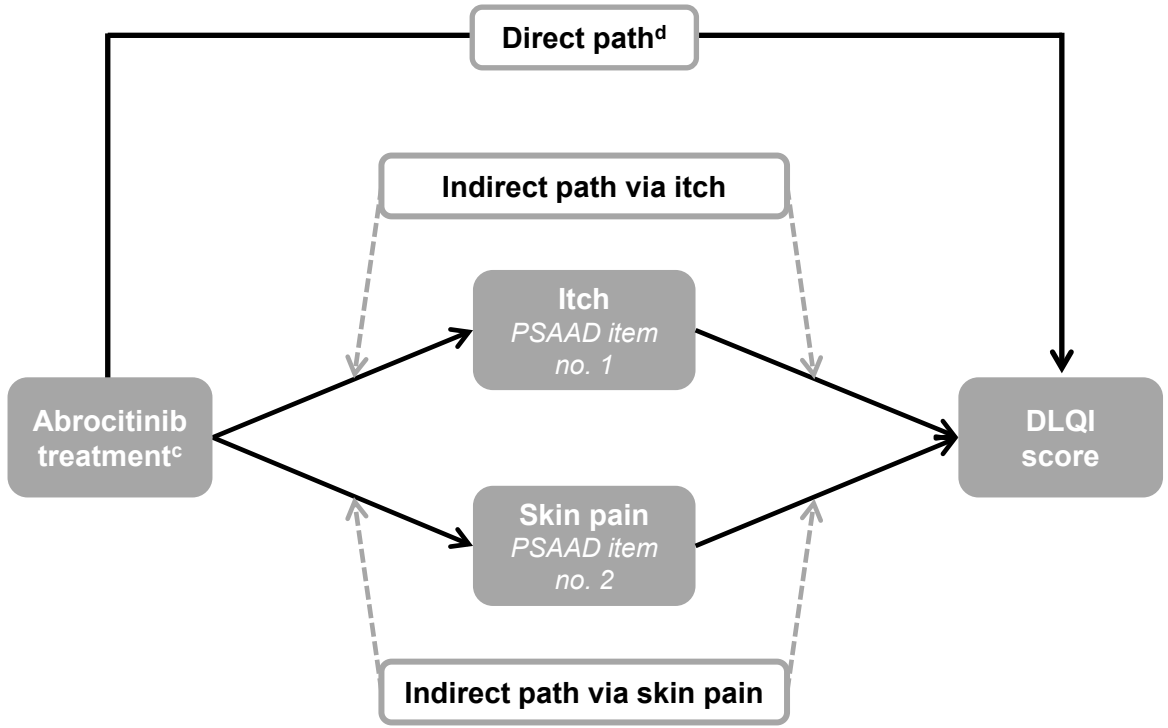
Methods

Patients

- Data from adult patients treated with abrocitinib monotherapy (200 mg or 100 mg) or placebo in the JADE MONO-1 and JADE MONO-2 trials were pooled for this analysis

Mediation Modeling

- Outcome variable
  - Dermatology-specific QoL, assessed by DLQI score
- Mediator variables
  - Itch, evaluated using PSAAD item no. 1 ("*How itchy was your skin over the past 24 hours?*")[a]
  - Skin pain, evaluated using PSAAD item no. 2 ("*How painful was your skin over the past 24 hours?*")[b]
- 3 separate mediation models were run
  - The CSMM was run separately at weeks 2, 4, 8, and 12 using all available data at each time point
  - The LMM, which does not assume independence among measurements of itch, skin pain, and DLQI at each timepoint, was used to estimate relationships among all available data from all weeks simultaneously
  - Based on the results of the CSMM and LMM, a pseudo steady-state model, in which the relationship among variables was assumed to be the same across timepoints, was applied
- Effects with $P<0.05$ were considered statistically significant



[a]On an 11-point NRS ranging from 0 (not itchy) to 10 (extremely itchy); [b]On an 11-point NRS ranging from 0 (not painful) to 10 (extremely painful);
[c]Abrocitinib treatment is a binary variable representing abrocitinib versus placebo; [d]Direct path represents the effects of other factors not included in the model.
CSMM, cross-sectional mediation model; DLQI, Dermatology Life Quality Index; LMM, longitudinal mediation model; NRS, numerical rating scale; PSAAD, Pruritus and Symptoms Assessment for Atopic Dermatitis

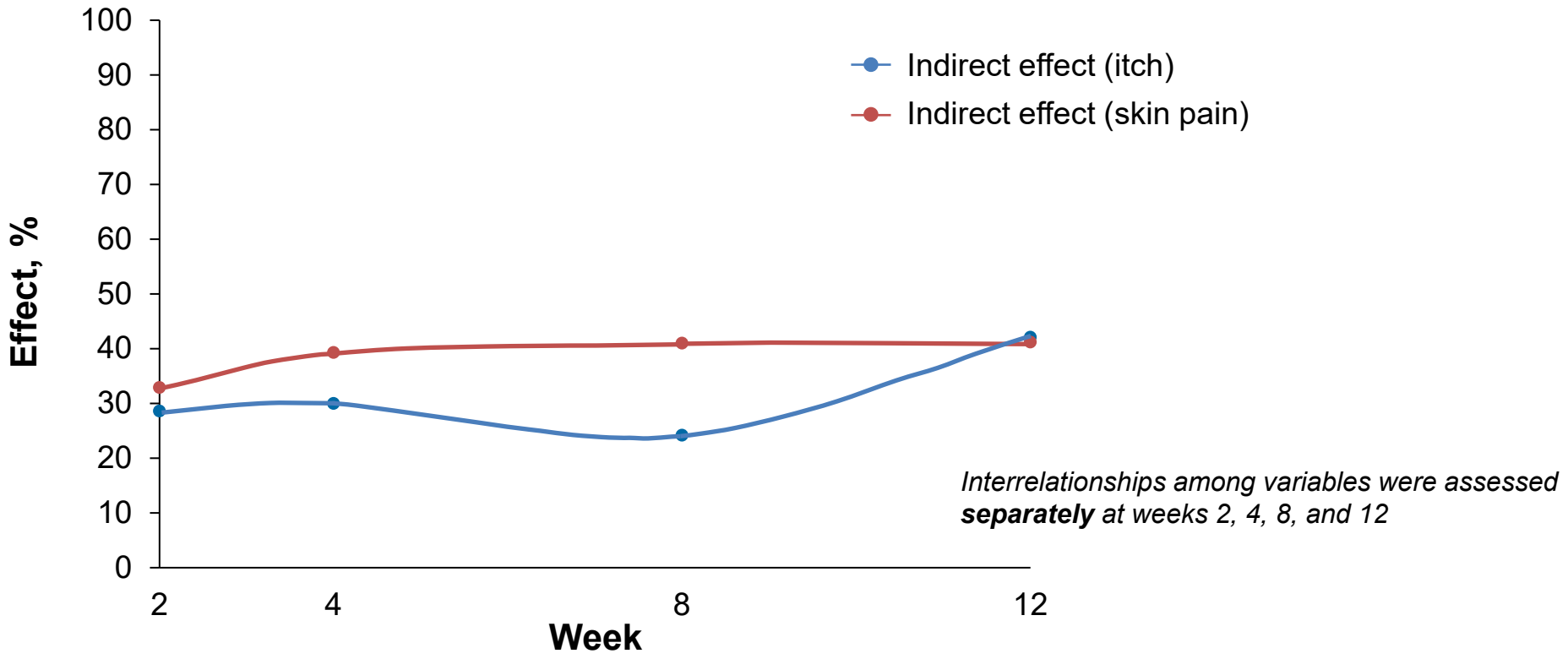
Baseline Characteristics

	JADE MONO-1 and JADE MONO-2 Adults N=654
Age, years, mean ± SD	37.4 ± 14.4
Duration of AD, years, mean ± SD	24.0 ± 15.6
IGA score, n (%) Moderate (IGA = 3) Severe (IGA = 4)	 431 (66) 223 (34)
EASI, mean ± SD	28.8 ± 12.0
PP-NRS[a] Mean ± SD Median (IQR) Range	 7.0 ± 1.8 7.0 (6.0, 8.0) 2.0–10.0
PSAAD[b] Mean ± SD Median (IQR) Range	 5.4 ± 2.0 5.4 (3.7, 6.9) 0.5–10.0
DLQI[c] Mean ± SD Median (IQR) Range	 14.8 ± 6.8 14.0 (10.0, 19.0) 1.0–30.0

[a]Evaluable patients: 653. [b]Evaluable patients: 616. [c]Evaluable patients: 649.
EASI, Eczema Area and Severity Index; IGA, Investigator's Global Assessment; IQR, interquartile range; PP-NRS, Peak Pruritus Numerical Rating Scale (used with permission from Regeneron Pharmaceuticals, Inc., and Sanofi).

Results: Cross-Sectional Mediation Model

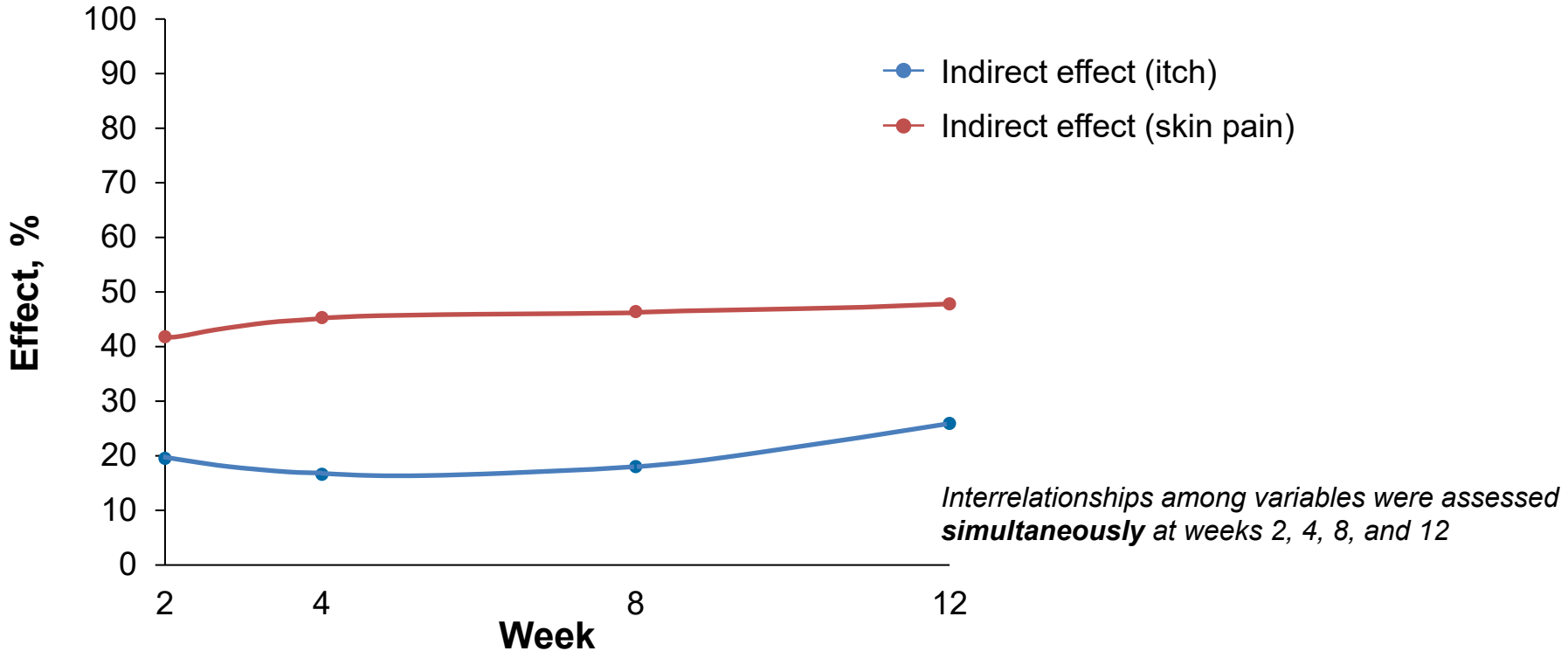
Estimated indirect effects of abrocitinib on DLQI over time mediated via itch or skin pain



- The indirect effect of abrocitinib treatment on DLQI score mediated via itch was considered approximately stable for the first 8 weeks before increasing at week 12
- The indirect effect mediated via skin pain was considered approximately stable from week 2 to week 12

Results: Longitudinal Mediation Model

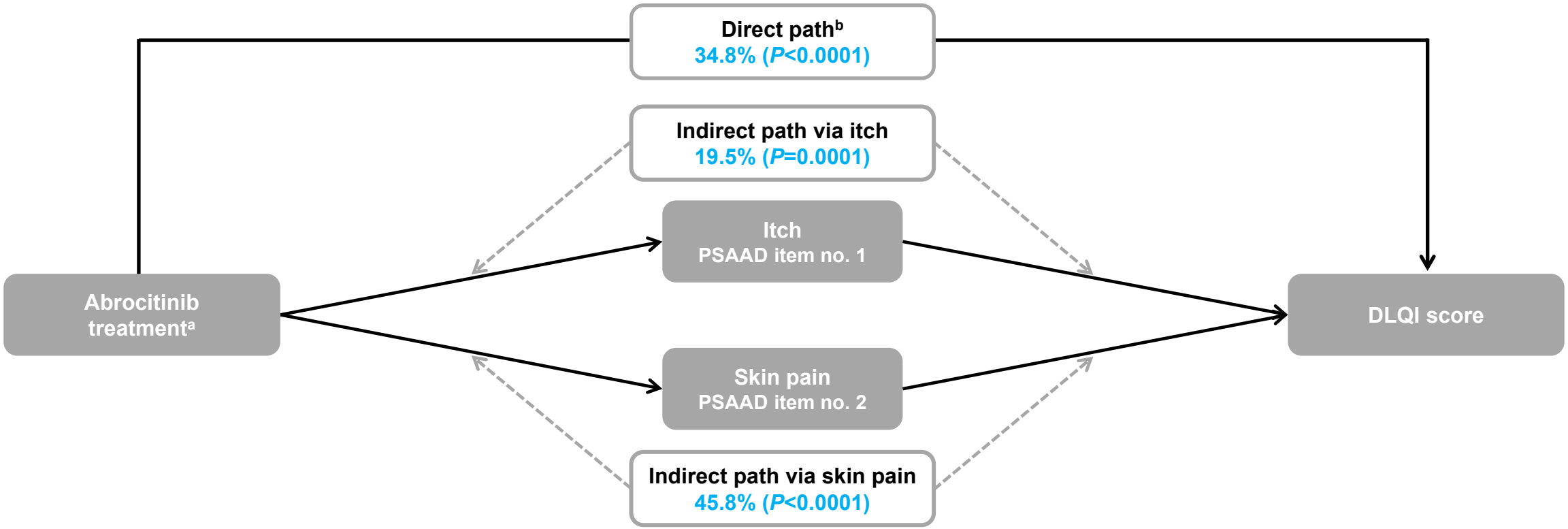
Estimated indirect effects of abrocitinib on DLQI over time mediated via itch or skin pain



- The indirect effect of abrocitinib treatment on DLQI score mediated via both itch and skin pain was considered approximately stable from week 2 to week 12

Results: Pseudo Steady-State Model

- The CSMM and LMM were generally consistent and indicated a pseudo steady-state period between weeks 2 and 12
- Using the pseudo steady-state model, the indirect effects of abrocitinib treatment on DLQI score mediated via reduction in itch and skin pain were 20% and 46%, respectively, and the direct effect (representing effects other than itch and skin pain) was 35%



[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.

Conclusions

- Improvements in dermatology-specific QoL with abrocitinib are mostly mediated indirectly via reduction in skin pain and less so by relief of itch
- Findings from this mediation analysis underscore the importance of skin pain as a symptom in AD
- Further research is warranted to examine how itch and skin pain can independently impact dermatology-specific QoL