Interpreting the Relationship Between Pruritus and Quality of Life in Patients With Moderate-to-Severe Atopic Dermatitis: A Post Hoc Analysis of JADE MONO-1 and JADE MONO-2

Melinda J. Gooderham,[1] Gil Yosipovitch,[2] Sonja Ständer,[3] Luz Fonacier,[4] Jacek C. Szepietowski,[5] Mette Deleuran,[6] Giampiero Girolomoni,[7] Andrew G. Bushmakin,[8] Joseph C. Cappelleri,[8] Melissa Watkins,[9] Claire Feeney,[10] Hernan Valdez,[9] Ricardo Rojo,[8] Marco DiBonaventura,[9] Daniela E. Myers[11]

[1]SKiN Centre for Dermatology, Peterborough, ON, Canada; [2]Miami Itch Center, Miller School of Medicine, University of Miami, Miami, FL, USA; [3]Center for Chronic Pruritus, Münster University Hospital, Münster, Germany; [4]NYU Langone Hospital–Long Island, Mineola, NY, USA; [5]Wroclaw Medical University, Wroclaw, Poland; [6]Aarhus University Hospital, Aarhus, Denmark; [7]University of Verona, Verona, Italy; [8]Pfizer Inc., Groton, CT, USA; [9]Pfizer Inc., New York, NY, USA; [10]Pfizer Ltd., Surrey, United Kingdom; [11]Pfizer Inc., Collegeville, PA, USA

BACKGROUND

- Atopic dermatitis (AD) is a chronic inflammatory skin disease associated with intense pruritus, which is the most burdensome symptom of AD[1] and has a profoundly adverse impact on health-related quality of life (HRQoL)[1,2]
- Abrocitinib is an oral once-daily Janus kinase 1 selective inhibitor under investigation for the treatment of moderate-to-severe AD[3,4]
- In 2 identical phase 3 studies (JADE MONO-1, NCT03349060; JADE MONO-2, NCT03575871), abrocitinib was shown to rapidly reduce pruritus in patients with moderate-to-severe AD, with higher proportions of patients achieving a clinically important itch response at week 2 (≥4-point improvement in Peak Pruritus Numerical Rating Scale score [PP-NRS4]; the PP-NRS is used with permission of Regeneron Pharmaceuticals, Inc., and Sanofi) compared with placebo at week 2[3,4]
  - Additionally, compared with placebo, abrocitinb improved HRQoL (as measured by the Dermatology Life Quality Index [DLQI], a dermatology-specific measure of HRQoL) in these trials[3,4]
- An association between pruritus (as measured by the Severity of Pruritus Scale [SPS]) and QoL in AD was previously reported[5]; however, the relationship between pruritus and dermatology-specific or general HRQoL is unclear

OBJECTIVE

- To quantify the relationship between pruritus severity and HRQoL in patients with moderate-to-severe AD

METHODS

Study Design and Patients

- This post hoc analysis included data from 2 randomized, placebo-controlled, phase 3 studies (JADE MONO-1 and JADE MONO-2)
- Patients enrolled in the studies were aged ≥12 years with
  - A clinical diagnosis of moderate-to-severe AD for ≥1 year (Investigator's Global Assessment [IGA] score ≥3, Eczema Area and Severity Index [EASI] score ≥16, percentage of body surface area affected (%BSA) ≥10, PP-NRS4)[3,4]
  - A recent history (<6 months) of inadequate response to topical corticosteroids or to topical calcineurin inhibitors given for ≥4 weeks or inability to receive topical treatment because it was medically inadvisable[3,4]
- Eligible patients were randomly assigned 2:2:1 to receive abrocitinib (200 mg or 100 mg) or placebo once daily for 12 weeks[3,4]
- Pruritus severity was assessed using the 10-point PP-NRS daily during the first 2 weeks of the study, then as single measurements at weeks 4, 8, and 12
- Dermatology-related HRQoL was assessed using the 10-question DLQI at baseline and at weeks 2, 4, 8, and 12
- General HRQoL was assessed using the SF-36v2 Health Survey (QualityMetrics) at baseline and at week 12
- Data from adult patients (≥18 years) from the abrocitinib and placebo arms were pooled across both trials

Interpreting the Relationship Between Pruritus and QoL and Function

- A repeated-measures longitudinal model was used to estimate the relationship between pruritus severity (using the PP-NRS as the predictor) and HRQoL (outcome)
- The outcome was either a DLQI total score or an SF-36 score
  - The SF-36 measures 8 health domains (physical functioning [PF], role participation with physical health problems [role-physical, RP], bodily pain [BP], general health [GH], vitality [VT], social functioning [SF], role participation with emotional health problems [role-emotional, RE], and mental health [MH]) and can be summarized as 2 summary scores (physical component summary [PCS] and mental component summary [MCS])
  - SF-36 norm-based standardized T scores (with a mean of 50 and a standard deviation of 10 reflecting normative scores for the US general population) were used
- To assess the validity of the linear approximation of the relationship between predictor and outcome, the model was also implemented with the PP-NRS as a categorical variable, which does not impose any functional relationship between predictor and outcome
- Clinically important change (CIC) in DLQI and SF-36 scores were based on Basra et al (DLQI)[6] and Optum's 1998 US general population sample normative data set (SF-36)[7]

RESULTS

Demographics and Baseline Disease Characteristics

Table 1. Significant Impairment in QoL in Patients With Moderate-to-Severe AD

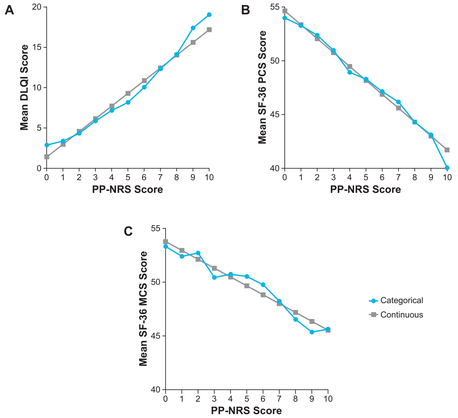
	JADE MONO-1 and JADE MONO-2 Pooled Adult Population N=654
Age group 18 to <65 years, n (%) ≥65 years, n (%) Median (Q1, Q3), y	 619 (94.6) 35 (5.4) 34.0 (26.0, 47.0)
Sex, n (%) Male	 381 (58.3)
Disease duration, median (Q1, Q3), y	22.6 (11.2, 33.2)
IGA, % Moderate (3) Severe (4)	 431 (65.9) 223 (34.1)
EASI, median (Q1, Q3)	24.9 (19.7, 35.4)
%BSA, median (Q1, Q3)	44.0 (30.5, 65.0)
PP-NRS, median (Q1, Q3)[a]	7.0 (6.0, 8.0)
DLQI, median (Q1, Q3)[b]	14.0 (10.0, 19.0)
SF-36 PCS, median (Q1, Q3)[c]	46.7 (40.3, 52.3)
SF-36 MCS, median (Q1, Q3)[c]	50.8 (42.0, 56.4)

%BSA, percentage of body surface area affected; DLQI, Dermatology Life Quality Index; EASI, Eczema Area and Severity Index; IGA, Investigator's Global Assessment; MCS, mental component summary; PCS, physical component summary; PP-NRS, Peak Pruritus Numerical Rating Scale.
[a]Baseline PP-NRS data available for 653 patients.
[b]Baseline DLQI data available for 649 patients.
[c]Baseline SF-36 data available for 652 patients.

Relationship Between Pruritus and HRQoL

- Data from 654 and 642 patients were available for the DLQI and SF-36 analyses, respectively
- Approximately linear relationships were observed between PP-NRS scores and
  - DLQI scores, indicating a direct association between severity of itch and dermatology-specific HRQoL (**Figure 1A**)
  - SF-36 domain and summary scores, indicating a direct association between severity of itch and general HRQoL (**Figures 1B**, **1C** represent relationships between PP-NRS and PCS and MCS; relationships between PP-NRS and other SF-36 domains had the same pattern)

Figure 1. Relationships Between PP-NRS Score and (A) DLQI Score, (B) SF-36 PCS Score, and (C) SF-36 MCS Score

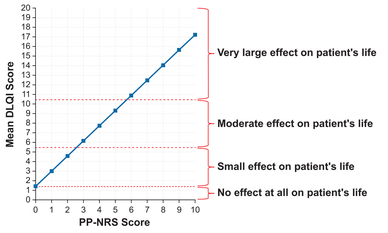


DLQI, Dermatology Life Quality Index; MCS, mental component summary; PCS, physical component summary; PP-NRS, Peak Pruritus Numerical Rating Scale.

Interpretation of the Relationship Between Pruritus Severity and HRQoL

- PP-NRS scores of 0, 1-2, 3-5, and ≥6 were associated with no, small, moderate, and very large effects, respectively, on dermatology-specific HRQoL, as measured by the DLQI (**Figure 2**)
- PP-NRS scores of ≤1 were associated with higher than US general population norms adjusted for age and sex for all SF-36 domains except GH (**Table 2**)
- PP-NRS scores of >5 were associated with lower than US general population norms adjusted for age and sex for all domains (**Table 2**)

Figure 2. Pruritus Severity Impacts Dermatology-Specific HRQoL



DLQI, Dermatology Life Quality Index; PP-NRS, Peak Pruritus Numerical Rating Scale.

Table 2. Interpretation of the Relationship Between Pruritus Severity and General HRQoL

		SF-36 Domain									
		PF	RP	BP	GH	VT	SF	RE	MH	PCS	MCS
SF-36 domain norms[a]		52.1	51.7	51.2	50.8	50.0	50.4	50.8	49.7	51.9	49.5
PP-NRS score	0	55.1	53.9	57.1	50.7	56.8	54.6	53.0	54.1	54.7	53.8
	1	54.4	52.6	55.3	49.8	55.7	53.3	52.3	53.3	53.4	53.0
	2	53.7	51.3	53.4	48.8	54.5	51.9	51.6	52.5	52.1	52.1
	3	53.0	50.0	51.5	47.8	53.4	50.6	50.9	51.6	50.8	51.3
	4	52.3	48.7	49.7	46.8	52.2	49.3	50.2	50.8	49.5	50.5
	5	51.6	47.4	47.8	45.8	51.1	47.9	49.5	49.9	48.2	49.7
	6	50.9	46.1	46.0	44.9	49.9	46.6	48.8	49.1	46.9	48.8
	7	50.2	44.8	44.1	43.9	48.7	45.3	48.1	48.3	45.6	48.0
	8	49.5	43.5	42.3	42.9	47.6	43.9	47.4	47.4	44.3	47.2
	9	48.8	42.2	40.4	41.9	46.4	42.6	46.7	46.6	43.0	46.4
	10	48.1	40.9	38.5	40.9	45.3	41.2	46.0	45.7	41.7	45.5

BP, bodily pain; GH, general health; MCS, mental component summary; MH, mental health; PCS, physical component summary; PF, physical functioning; PP-NRS, Peak Pruritus Numerical Rating Scale; RE, role-emotional; RP, role-physical; SF, social functioning; VT, vitality.
[a]SF-36 domain norms adjusted for age and sex; highlighted values represent domain scores that are better than adjusted norms.

Responder-Level Interpretation of the Relationship Between Pruritus and HRQoL

- On average, a 3-point improvement in PP-NRS score (PP-NRS3) was associated with improvements larger than the CIC in
  - DLQI score (PP-NRS3 is associated with a 4.7-point improvement in total DLQI score, which is larger than the DLQI CIC of 4 points; **Table 3**)
  - RP (PP-NRS3 is associated with a 3.9-point improvement in RP; the RP CIC = 3.2 points) and BP (PP-NRS3 is associated with a 5.6-point improvement in BP; the BP CIC = 4.5 points) domains and PCS (PP-NRS3 is associated with a 3.9-point improvement in PCS; the PCS CIC = 3.1 points) score on the SF-36 (**Table 3**)
- On average, a PP-NRS4 response is associated with a 5.4-point improvement in the SF domain score, which is larger than the SF CIC of 5.0 points

Table 3. Improvement in PP-NRS Score Is Associated With Improvement in HRQoL

			SF-36 Domain									
		DLQI	PF	RP	BP	GH	VT	SF	RE	MH	PCS	MCS
Established CIC[a]		−4.0	3.5	3.2	4.5	5.7	5.5	5.0	3.8	5.5	3.1	3.8
Point improvement in PP-NRS	1	−1.6	0.7	1.3	1.9	1.0	1.2	1.3	0.7	0.8	1.3	0.8
	2	−3.2	1.4	2.6	3.7	2.0	2.3	2.7	1.4	1.7	2.6	1.7
	3	−4.7	2.1	3.9	5.6	2.9	3.5	4.0	2.1	2.5	3.9	2.5
	4	−6.3	2.8	5.2	7.4	3.9	4.6	5.4	2.8	3.4	5.2	3.3
	5	−7.9	3.5	6.5	9.3	4.9	5.8	6.7	3.5	4.2	6.5	4.1
	6	−9.5	4.2	7.8	11.1	5.9	6.9	8.0	4.2	5.0	7.8	5.0
	7	−11.1	4.9	9.1	13.0	6.8	8.1	9.4	4.9	5.9	9.1	5.8
	8	−12.6	5.6	10.4	14.8	7.8	9.2	10.7	5.6	6.7	10.4	6.6
	9	−14.2	6.3	11.7	16.7	8.8	10.4	12.0	6.3	7.6	11.7	7.4
	10	−15.8	7.0	13.0	18.6	9.8	11.5	13.4	7.0	8.4	13.0	8.3

BP, bodily pain; CIC, clinically important change; DLQI, Dermatology Life Quality Index; GH, general health; MCS, mental component summary; MH, mental health; PCS, physical component summary; PF, physical functioning; PP-NRS, Peak Pruritus Numerical Rating Scale; RE, role-emotional; RP, role-physical; SF, social functioning; VT, vitality.
[a]Responder-level CIC based on Basra et al (DLQI)[6] and Optum's 1998 US general population sample normative data set (SF-36)[7]; highlighted values represent CICs for PP-NRS3 and PP-NRS4 response.

CONCLUSIONS

- The severity of itch as assessed by the PP-NRS was strongly associated with HRQoL as measured by the DLQI and SF-36 in this post hoc analysis of patients with moderate-to-severe AD in JADE MONO-1 and JADE MONO-2
- Although the threshold for CIC in pruritus used in clinical trials is a 4-point improvement in PP-NRS score, the current analyses suggest that a 3-point change might be sufficient for a CIC in HRQoL as measured by the DLQI and the RP and BP domains and the PCS scores of the SF-36

REFERENCES

1. Silverberg JI et al. *Ann Allergy Asthma Immunol.* 2018;121:340-347.
2. Kini SP et al. *Arch Dermatol.* 2011;147:1153-1156.
3. Simpson EL et al. *Lancet.* 2020;396:255-266.
4. Silverberg JI et al. *JAMA Dermatol.* 2020;156:863-873.
5. Stander S et al. *J Eur Acad Dermatol Venereol.* 2019;33:1742-1746.
6. Basra MK et al. *Dermatology.* 2015;230:27-33.
7. Ware J et al. Development. User's Manual for the SF-36v2® Health Survey. Johnstown, RI: QualityMetric Incorporated.

ACKNOWLEDGMENTS

Editorial/medical writing support under the guidance of the authors was provided by Megan Elder, PhD, at ApotheCom, San Francisco, CA, USA, and was funded by Pfizer Inc., New York, NY, USA, in accordance with Good Publication Practice (GPP3) guidelines (*Ann Intern Med.* 2015;163:461-464).

These studies were sponsored by Pfizer Inc.

Presented at the RAD Virtual Conference; June 13, 2021