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ORIGINAL RESEARCH ARTICLE

Impact of Oral Abrocitinib Monotherapy on Patient-Reported Symptoms and Quality of Life in Adolescents and Adults with Moderate-to-Severe Atopic Dermatitis: A Pooled Analysis of Patient-Reported Outcomes

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Abstract

Background Atopic dermatitis imparts a substantial patient burden, including itch, sleep disturbance, and decreased health-related quality of life.

Objective This analysis evaluated changes in patient-reported outcomes of disease-specific signs/symptoms and health-related quality of life in adult and adolescent patients with moderate-to-severe atopic dermatitis treated with once-daily oral abrocitinib 200-mg or 100-mg monotherapy.

Methods Pooled data from one phase IIb (NCT02780167) and two phase III (NCT03349060, JADE MONO-1; NCT03575871, JADE MONO-2) monotherapy trials in adult and adolescent patients with moderate-to-severe atopic dermatitis were analyzed. Patient-reported outcome assessments included: global severity, itch, and multi-item measures that assess other signs and symptoms of atopic dermatitis. Additional patient-reported outcome assessments measured depression, anxiety, fatigue, disease-specific and general health-related quality of life, and work and general productivity among employed patients.

Results Overall, 942 patients were included in this analysis. Improvements were observed from the first post-baseline assessment to week 12 across all patient-reported outcomes, including Patient Global Assessment (PtGA) score of 0/1 (35.5%, 19.8%, and 5.9% for 200 mg, 100 mg, and placebo, respectively), ≥ 4-point improvement in Night Time Itch Scale (NTIS; 57.0%, 42.7%, and 12.7%), change from baseline in Patient-Oriented Eczema Measure (POEM) score (− 11.4, − 8.2, and − 3.4), 1-point improvement in Pruritus and Symptoms Assessment for Atopic Dermatitis (PSAAD; 75.2%, 65.1%, and 33.5%), Hospital Anxiety and Depression Scales (HADS) anxiety (− 2.0, − 1.7, and − 1.0) and depression (− 1.7, − 1.3, and − 0.1).

Conclusions Abrocitinib monotherapy improved disease-specific signs/symptoms and health-related quality of life across multiple domains as reported by adult and adolescent patients with moderate-to-severe atopic dermatitis, complementing clinician-reported efficacy and safety outcomes.

Clinical Trial Registration NCT02780167 (registered 23 May, 2016), NCT03349060 (registered 21 November, 2017), NCT03575871 (registered 3 July, 2018).

1 Introduction

Atopic dermatitis (AD) is a chronic, relapsing, inflammatory skin condition with a high disease and comorbidity burden that affects up to 20% of children and 5–10% of adults worldwide [1–5]. Moderate-to-severe AD negatively affects patient health-related quality of life (HRQoL), impacting patients, their finances, families, and society in general [6–8]. Pruritus is the most common and bothersome symptom of AD [4, 9] and is associated with sleep disturbance [10], which additionally may lead to psychological comorbidities, including anxiety, depression, and fatigue [11–16]. Atopic dermatitis is also associated with a higher work absentee rate, causing substantial direct and indirect costs [17].

Abrocitinib is an oral, once-daily, Janus kinase 1 (JAK1) selective inhibitor under investigation for the treatment of moderate-to-severe AD. By selectively inhibiting JAK1,

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Key Points

Abrocitinib, an oral, once-daily, Janus kinase 1 selective inhibitor, showed efficacy and a manageable safety profile for adult and adolescent patients with moderate-to-severe atopic dermatitis in phase IIb and III trials; this analysis focuses on patient-report outcome assessments in phase IIb and phase III monotherapy trials.

The pooled analysis from three monotherapy studies (N = 942) showed that adults and adolescents with moderate-to-severe atopic dermatitis treated with abrocitinib experienced clinically meaningful improvements in all patient-reported outcomes, especially itch, depression/anxiety, fatigue, and work productivity, which represent some of the most burdensome impacts of atopic dermatitis. Improvements in itch, sleep disturbance, skin pain, and health-related quality of life were evident as early as week 2 and sustained over a period of 12 weeks.

These results provide important information on the efficacy of abrocitinib from the patient perspective and complement clinician-reported efficacy and safety outcomes from previous phase IIb and III monotherapy trials.

abrocitinib modulates the signaling pathways of several key cytokines involved in the pathogenesis of AD and pruritus [18]. Monotherapy with once-daily oral abrocitinib showed significant efficacy in three phase II/III placebo-controlled trials in adolescents and adults with moderate-to-severe AD [19–21]. A phase IIb trial in adults with moderate-to-severe AD showed that abrocitinib was safe and effective in reducing signs and symptoms of AD based on Investigator's Global Assessment (IGA) response (clear [0] or almost clear [1] with ≥ 2-grade improvement) and change in Eczema Area and Severity Index (EASI) score from baseline [19]. In JADE MONO-1, significantly greater proportions of abrocitinib-treated (200 mg or 100 mg) patients than placebo-treated patients achieved IGA response (43.8% and 23.7% vs 7.9%; $p < 0.0001$ and $p < 0.005$, respectively) and/or ≥ 75% improvement in EASI (EASI-75) response (62.7% and 39.7% vs 11.8%; $p < 0.0001$ for both) [20]. Likewise, in JADE MONO-2, greater proportions of abrocitinib-treated (200 mg or 100 mg) than placebo-treated patients achieved IGA response (38.1%, 28.4% vs 9.1%; $p < 0.001$) and/or EASI-75 response (61.0%, 44.5% vs 10.4%; $p < 0.0001$) [21].

Although it is important to establish efficacy and safety for new treatments, clinician-reported outcome assessments do not capture the full extent of treatment benefits experienced by patients; therefore, it is important to report the clinically relevant and complementary data captured by patient-reported outcome (PRO) assessments from clinical trials [22, 23]. Hence, to generate a comprehensive assessment of the effect of a treatment on AD, the Harmonising Outcome Measures for Eczema and the More Than Skin Deep initiatives have recommended that clinical trials in AD include assessments of patient-reported symptoms, particularly Patient-Oriented Eczema Measure (POEM) and Pruritus Numerical Rating Scale (Pruritus-NRS)/Peak Pruritus Numerical Rating Scale (PP-NRS), and HRQoL, particularly the Dermatology Life Quality Index (DLQI), alongside clinician-evaluated endpoints and long-term disease control, as core outcome measures [24, 25]. Here, we present a pooled analysis from the placebo-controlled phase IIb and III studies of the effect of abrocitinib monotherapy on PRO measures in adolescents and adults with moderate-to-severe AD.

2 Methods

2.1 Study Designs

All three studies included in this pooled analysis were similarly designed, international, multicenter, randomized, double-blind, placebo-controlled, parallel-group trials (Table 1 of the Electronic Supplementary Material [ESM]). The phase IIb study (NCT02780167) was conducted between April 2016 and April 2017 in Australia, Canada, Germany, Hungary, and the USA [19]. JADE MONO-1 (NCT03349060) was a phase III trial conducted between December 2017 and March 2019 in Australia, Canada, Europe, and the USA [20]. JADE MONO-2 (NCT03575871) was a phase III trial conducted between June 2018 and August 2019 in Australia, Canada, China, Europe, Japan, South Korea, and the USA [21].

All studies had similar eligibility criteria (described previously [19–21]). Briefly, eligible patients were either 18–75 years of age (phase IIb) or ≥ 12 years of age (phase III) with moderate-to-severe AD (IGA ≥ 3, EASI [26] score ≥12 [phase IIb] or ≥ 16 [phase III], affected percentage of body surface area ≥ 10, PP-NRS [27] (used with permission of Regeneron Pharmaceuticals, Inc. and Sanofi) score ≥ 4 [PP-NRS4; phase III only], and inadequate response to treatment with topical corticosteroids or topical calcineurin inhibitors given for ≥ 4 weeks, a history of topical AD treatments considered medically inadvisable, or a history of systemic therapies for AD. Exclusion criteria were medical history of conditions associated with thrombocytopenia, coagulopathy, or platelet dysfunction; prior systemic JAK inhibitor use; systemic corticosteroid use within 4 weeks of study initiation; and treatment with dupilumab within 6 weeks of study initiation. The phase III studies also excluded patients with suicidal ideation associated with actual intent and method

or plan in the past year (Columbia Suicide Severity Rating Scale [C-SSRS] [28] items 4 and 5), history of suicidal behaviors in the past 5 years (any CSSRS suicidal behavior item in the past 5 years), lifetime history of serious or recurrent suicidal behavior (Suicidal Behaviors Questionnaire-Revised [29] total score ≥ 8), clinically significant depression (Patient Health Questionnaire-8 [30] total score ≥ 15), or any other major psychiatric disorder that might require exclusion in the opinion of the investigator. Use of topical medicated therapies for AD (topical corticosteroids, topical calcineurin inhibitors, tars, antibiotic creams, topical antihistamines) and rescue medication (e.g., oral corticosteroids) was not permitted, but patients were allowed to use oral antihistamines and/or topical nonmedicated emollients during the studies.

In the phase IIb study, patients were randomly assigned 1:1:1:1:1 to receive once-daily oral abrocitinib 200 mg, abrocitinib 100 mg, abrocitinib 30 mg, abrocitinib 10 mg, or matching placebo for 12 weeks. In the phase III studies, patients were randomly assigned 2:2:1 (stratified by baseline disease severity [IGA 3 or 4] and age group [12 to < 18 years or ≥ 18 years]) to receive once-daily oral abrocitinib 200 mg, abrocitinib 100 mg, or matching placebo for 12 weeks. This analysis includes patients randomly assigned to receive abrocitinib 200 mg, abrocitinib 100 mg, or placebo.

2.2 Assessments

Patient-reported outcome assessments in all three studies included proportions of patients achieving a ≥ 4-point improvement in itch score (PP-NRS and Pruritus-NRS) [27, 31]. Other PRO assessments included in all studies were: Patient Global Assessment (PtGA) [32, 33] clear or almost clear with a ≥ 2-point improvement; Pruritus and Symptoms Assessment for Atopic Dermatitis (PSAAD [33]) total score; change from baseline in POEM [35–37] total score; distributions of patients across DLQI [38] and Children's Dermatology Life Quality Index (CDLQI [39]) band descriptors; and change from baseline in Hospital Anxiety and Depression Scale (HADS) [40, 41] depression and/or anxiety subscale scores and, among patients with respective baseline subscale scores ≥ 8, proportions of patients achieving subscale scores < 8.

Several additional PRO endpoints were assessed in JADE MONO-1/MONO-2, including change from baseline in the Short Form-36 Health Survey, Version 2, Acute (SF-36v2) [42] mental and physical component summary scores and domain scores (for patients aged ≥ 18 years only), EuroQol 5-Dimension 5-Level Scale (EQ-5D-5L) [43] or EuroQol 5-Dimension Youth Scale (EQ-5D-Y) [44] index score, and Functional Assessment of Chronic Illness Therapy Fatigue Scale (FACIT-F) [45] score or Pediatric FACIT-F (Peds-FACIT-F) [46] score as well as the proportion of patients achieving FACIT-F/Peds-FACIT-F < 30 at week 12 (among patients with FACIT-F/Peds-FACIT-F ≥ 30 at baseline).

JADE MONO-2 assessed two additional PRO endpoints: change from baseline in Work Productivity and Activity Impairment Questionnaire–Atopic Dermatitis, Version 2.0 (WPAI-AD) [47] score (for patients aged ≥ 18 years only) and the proportion of patients and time to achieve a ≥ 4-point improvement in Night Time Itch Scale (NTIS) score for severity of worst itching due to AD during the previous night's sleep. More detailed descriptions of each PRO assessment are summarized in Table 1.

2.3 Statistical Analysis

Binary endpoints were analyzed using the Cochran–Mantel–Haenszel test adjusted by randomization strata. Missing responses for patients who permanently discontinued the study were defined as non-responders at all subsequent visits. Continuous endpoints were analyzed based on the observed data using mixed-model repeated measures with fixed factors of treatment, week, treatment-by-week interaction, study, baseline disease severity, age category, and baseline value and unstructured covariance matrix or compound symmetry covariance matrix.

3 Results

3.1 Demographics and Baseline Disease Characteristics

Overall, 942 patients were included in this pooled analysis. Baseline disease characteristics were similar across treatment groups and across three included studies (Table 2 and Supplementary Table 2 of the ESM). The total population reported moderate-to-severe signs and symptoms of AD per mean POEM total score (Table 3). Furthermore, 62.7% of patients had moderate AD and 37.3% had severe AD per IGA; this distribution was 43.7% and 48.7%, respectively, per PtGA (Table 3). Finally, the patients reported considerable symptoms of anxiety or depression per HADS subscores and a very large effect of AD on their quality of life (QoL) based on mean DLQI and CDLQI total scores (Table 3).

3.2 Symptoms of AD

Mean (standard deviation [SD]) Pruritus-NRS (phase IIb)/PP-NRS scores (phase III; 200 mg, 100 mg, and placebo) were 7.0 (1.9), 7.1 (1.9), and 7.0 (1.9) at baseline and 2.9 (2.6), 3.9 (2.7), 5.4 (2.6) at week 12, respectively. Pooled proportions of patients achieving a ≥ 4-point improvement in itch severity based on Pruritus-NRS/PP-NRS score were greater starting at the first post-baseline assessment (week 2) for abrocitinib 200

Table 1 Summary of patient-reported outcomes evaluated in this analysis

Patient-reported outcomes	Descriptions	Assessments
PP-NRS [27]	Self-report of worst itch in the last 24 h Scores range from 0 to 10, with higher scores indicating worse itch Minimal clinically important difference is a ≥ 2–4 point change from baseline	Assessed during screening and daily on days 1–15 and on study visit days thereafter for phase III studies
Pruritus-NRS [31]	Self-report of itch in the last 24 hours Scores range from 0 to 10, with higher scores indicating worse itch	Assessed daily on days 1–15 and on study visit days thereafter for the phase IIb study
PtGA [32, 33]	Scores range from 0 (clear) to 4 (severe), with higher scores indicating worse self-reported cutaneous disease	Assessed on study visit days
PSAAD [34]	Scores range from 0 to 10, with higher scores indicating worse daily symptoms of AD Clinically important response defined as a ≥ 1-point improvement from baseline	Assessed on study visit days
POEM [35–37]	Scores range from 0 to 28, with higher scores indicating higher severity of AD	Assessed on study visit days
DLQI [38]	Scores range from 0 to 30, with higher scores indicating worse QoL For patients aged ≥ 18 years	Assessed on study visit days
CDLQI [39]	Scores range from 0 to 30, with higher scores indicating worse QoL For patients aged < 18 years	Assessed on study visit days
HADS [40, 41]	Scores range from 0 to 21, with higher scores indicating increased anxiety or depression	Assessed on study visit days
SF-36v2 [42]	Assessed on study visit days Norm-based scoring, with higher scores indicating higher impact on functional health and well-being	Assessed on study visit days
EQ-5D-5L [43]	Scores range from 1 to 5, with higher scores indicating increased problems For patients aged ≥ 18 years	Assessed on study visit days
EQ-5D-Y [44]	Scores range from 1 to 5, with higher scores indicating increased problems For patients aged < 18 years	Assessed on study visit days
FACIT-F [45]	Scores range from 0 to 4, with higher scores indicating less fatigue For patients aged ≥ 18 years	Assessed on study visit days
Peds-FACIT-F [46]	Scores range from 0 to 4, with higher scores indicating less fatigue For patients aged < 18 years	Assessed on study visit days
WPAI-AD [47]	Scores range from 0% to 100%, with higher scores indicating a greater percentage of work/activity time that was impaired For patients aged ≥ 18 years	Assessed on study visit days
NTIS	Scores range from 0 (no itch/never or no itching) to 10 (worst itch imaginable/always or constant itching), with higher scores indicating worse itch	Assessed on days 1–15 and on study visit days thereafter

AD atopic dermatitis, *CDLQI* Children's Dermatology Life Quality Index, *DLQI* Dermatology Life Quality Index, *EQ-5D-5L* EuroQol 5-Dimension 5-Level Scale, *EQ-5D-Y* EuroQol 5-Dimension Youth Scale, *FACIT-F* Functional Assessment of Chronic Illness Therapy Fatigue Scale, *HADS* Hospital Anxiety and Depression Scale, *NTIS* Night Time Itch Scale, *Peds-FACIT-F* Pediatric Functional Assessment of Chronic Illness Therapy Fatigue Scale, *POEM* Patient Oriented Eczema Measure, *PP-NRS* Peak Pruritus Numerical Rating Scale, *Pruritus-NRS* Pruritus Numerical Rating Scale, *PSAAD* Pruritus and Symptoms Assessment for Atopic Dermatitis, *PtGA* Patient Global Assessment, *QoL* quality of life, *SF-36v2* Short Form-36 Health Survey, Version 2, Acute, *WPAI-AD* Work Productivity and Activity Impairment Questionnaire–Atopic Dermatitis, Version 2.0

Table 2 Baseline demographic characteristics

	Placebo	Abrocitinib		Total
		100 mg	200 mg	
Pooled monotherapy (phase IIb/III)	*N* = 216	*N* = 369	*N* = 363	*N* = 942
Age, mean (SD), years	35.0 (15.0)	35.9 (15.8)	34.1 (16.4)	35.0 (15.9)
Age group, *n* (%)				
12–17 years	25 (11.9)	51 (13.8)	48 (13.2)	124 (13.2)
18–64 years	178 (84.8)	297 (80.5)	289 (79.6)	764 (81.1)
≥ 65 years	7 (3.3)	21 (5.7)	26 (7.2)	54 (5.7)
Male sex, *n* (%)	117 (55.7)	215 (58.3)	197 (54.3)	529 (56.2)
Race, *n* (%)				
White	141 (67.1)	253 (68.6)	231 (63.6)	625 (66.3)
Asian	39 (18.6)	80 (21.7)	85 (23.4)	204 (21.7)
Black or African American	22 (10.5)	31 (8.4)	30 (8.3)	83 (8.8)
Multiracial	2 (1.0)	2 (0.5)	8 (2.2)	12 (1.3)
Other	3 (1.4)	2 (0.5)	5 (1.4)	10 (1.1)
Not reported	3 (1.4)	1 (0.3)	4 (1.1)	8 (0.8)
Ethnicity, *n* (%)				
Not Hispanic or Latino (of any race)	196 (93.3)	352 (95.4)	349 (96.1)	897 (95.2)
Hispanic or Latino (of any race)	11 (5.2)	14 (3.8)	12 (3.3)	37 (3.9)
Not reported	3 (1.4)	3 (0.8)	2 (0.6)	8 (0.8)

SD standard deviation

mg and 100 mg compared with placebo. At week 2, 44.2% (200 mg), 24.9% (100 mg), and 5.8% (placebo) of patients achieved a ≥ 4-point improvement (i.e., response criteria in phase III studies). Proportions achieving a ≥ 4-point improvement in Pruritus-NRS/PP-NRS at weeks 4, 8, and 12 were, respectively, 57.5%, 59.2%, and 57.3% for 200 mg, 35.7%, 39.7%, and 42.9% for 100 mg, and 12.3%, 14.3%, and 16.5% for placebo. Similarly, a significant proportion of patients achieved an itch-free or virtually itch-free status (i.e., PP-NRS 0/1) at week 12 with abrocitinib 200 mg or 100 mg (36.6% and 23.4%, respectively) compared with placebo (5.3%). The median (95% confidence interval [CI]) time to achieve a ≥4-point improvement in Pruritus-NRS/PP-NRS was significantly shorter for abrocitinib 200 mg (15 days [13–29]) and abrocitinib 100 mg (57 days [30–64]) vs placebo (112 days [92–not estimable]).

Mean (SD) NTIS scores (200 mg, 100 mg, and placebo) were 6.8 (1.9), 6.8 (2.0), and 6.2 (2.1) at baseline and 2.2 (2.3), 3.2 (2.8), and 4.8 (3.0) at week 12, respectively. A higher proportion of patients receiving abrocitinib (100 or 200 mg) experienced a ≥ 4-point improvement in the severity of night-time itch (Fig. 1a). The differences in the proportion of patients who achieved NTIS response at week 12 vs placebo for abrocitinib 200 mg and 100 mg were 44.6% (95% CI 33.0–56.1; $p < 0.0001$) and 29.8% (95% CI 18.3–41.4; $p < 0.0001$), respectively. The median (95% CI) time to achieve a ≥ 4-point improvement in the NTIS score was significantly shorter for abrocitinib 200 mg (29 days [14–33]) and abrocitinib 100 mg (57 days [30–81]) vs placebo (116 days [89–116]; $p < 0.0001$ for both). Mean (SD) PSAAD scores (200 mg, 100 mg, and placebo) were 5.3 (2.1), 5.3 (2.2), and 5.3 (2.0) at baseline and 2.0 (2.1), 2.8 (2.1), and 4.3 (2.4) at week 12, respectively. Overall, > 50% of patients treated with abrocitinib reported experiencing a clinically important response in pruritus and symptoms as measured by PSAAD (≥ 1-point improvement) starting at week 2 and continuing through week 12; the proportions of responders were greater for both doses of abrocitinib than placebo at all time points (Fig. 1b). As measured with PtGA, the proportions of patients with moderate AD (200 mg, 100 mg, and placebo) were 46.6%, 38.5%, and 48.1% at baseline and 22.7%, 32.8%, and 31.6% at week 12, respectively. The proportions of patients with severe AD (200 mg, 100 mg, and placebo) were 46.3%, 53.1%, and 45.2% at baseline and 7.1%, 12.4%, and 23.9% at week 12, respectively. In the overall monotherapy pool, both doses of abrocitinib improved overall disease severity as rated by patients (PtGA) starting at the first post-baseline assessment (week 2) and continuing through the end of treatment (Fig. 1c). Mean (SD) POEM scores (200 mg, 100 mg, and placebo) were 19.8 (5.8), 20.2 (6.2), and 19.9 (5.8) at baseline and 8.9 (7.5), 12.0 (7.8), and 16.4 (7.1) at week 12, respectively. Compared with placebo-treated patients, abrocitinib-treated patients reported marked reductions in the frequency of symptoms via POEM throughout the study (Fig. 1d).

Table 3 Baseline disease characteristics

	Placebo	Abrocitinib		Total
		100 mg	200 mg	
Pooled monotherapy (phase IIb/III)	*N* = 216	*N* = 369	*N* = 363	*N* = 942
Disease duration, median (range), years	20.8 (1.1–67.1)	21.2 (1.0–68.6)	18.9 (1.0–68.8)	20.2 (1.0–68.8)
IGA, *n* (%)				
Moderate (3)	132 (62.9)	228 (61.8)	231 (63.6)	591 (62.7)
Severe (4)	78 (37.1)	141 (38.2)	132 (36.4)	351 (37.3)
EASI score, mean (SD)	27.6 (11.8)	29.4 (12.4)	29.0 (13.4)	28.8 (12.7)
%BSA, mean (SD)	45.8 (22.1)	48.6 (22.5)	47.2 (23.6)	47.4 (22.8)
Pruritus-NRS/PP-NRS score, mean (SD)	*n* = 207 7.0 (1.9)	*n* = 368 7.1 (1.9)	*n* = 362 7.0 (1.9)	*n* = 937 7.0 (1.9)
POEM total score, mean (SD)	*n* = 209 19.9 (5.8)	*n* = 362 20.2 (6.2)	*n* = 359 19.8 (5.8)	*n* = 930 20.0 (5.9)
PtGA, *n* (%)	*n* = 209	*n* = 362	*n* = 359	*n* = 930
Clear	0	1 (0.3)	0	1 (0.1)
Almost clear	5 (2.4)	3 (0.8)	2 (0.6)	10 (1.1)
Mild	8 (3.8)	23 (6.2)	21 (5.8)	52 (5.5)
Moderate	101 (48.1)	142 (38.5)	169 (46.6)	412 (43.7)
Severe	95 (45.2)	196 (53.1)	168 (46.3)	459 (48.7)
PSAAD total score, mean (SD)	*n* = 171 5.3 (2.0)	*n* = 314 5.3 (2.2)	*n* = 317 5.3 (2.1)	*n* = 802 5.3 (2.1)
HADS score, mean (SD)	*n* = 208	*n* = 362	*n* = 358	*n* = 928
Depression subscale	4.5 (3.6)	4.3 (4.0)	4.2 (3.8)	4.3 (3.8)
Anxiety subscale	6.6 (4.0)	6.0 (4.3)	5.8 (4.0)	6.1 (4.1)
DLQI total score,[a] mean (SD)	*n* = 184 14.3 (7.2)	*n* = 315 15.1 (7.1)	*n* = 311 14.4 (6.6)	*n* = 810 14.6 (6.9)
CDLQI total score,[b] mean (SD)	*n* = 24 12.5 (6.3)	*n* = 48 12.4 (6.4)	*n* = 47 13.1 (5.5)	*n* = 119 12.7 (6.0)
Pooled monotherapy (phase III)	*n* = 155	*n* = 314	*n* = 309	*n* = 778
FACIT-F score,[a] mean (SD)	37.9 (10.2)	37.4 (11.8)	38.3 (10.6)	37.9 (11.0)
Peds-FACIT-F score,[b] mean (SD)	35.8 (7.8)	36.2 (9.0)	37.1 (7.7)	36.5 (8.2)
EQ-5D-5L index score,[a] mean (SD)	0.78 (0.15)	0.79 (0.15)	0.80 (0.14)	0.79 (0.15)
EQ-5D-Y index score,[b] mean (SD)	0.63 (0.39)	0.66 (0.36)	0.65 (0.32)	0.65 (0.35)
SF-36v2 score,[a] mean (SD)				
Mental component summary	48.6 (9.2)	48.3 (10.8)	47.9 (10.7)	48.2 (10.4)
Physical component summary	46.0 (8.1)	45.2 (9.0)	46.0 (8.0)	45.7 (8.4)
JADE MONO-2 study				
WPAI-AD,[a] mean (SD)				
Percentage work time missed[c]	*n* = 42 4.2 (10.3)	*n* = 93 4.6 (16.0)	*n* = 79 5 (19.5)	*n* = 214 4.7 (16.4)
Percentage impairment while working[c]	*n* = 42 35.2 (24.3)	*n* = 92 35.4 (26.3)	*n* = 76 36.4 (26.3)	*n* = 210 35.8 (25.8)
Percentage overall work impairment[c]	*n* = 42 37.3 (25.8)	*n* = 92 36.4 (27.4)	*n* = 76 36.9 (26.6)	*n* = 210 36.8 (26.7)
Percentage activity impairment	*n* = 70 41.9 (27.2)	*n* = 139 41.0 (27.5)	*n* = 138 43.0 (25.6)	*n* = 347 42.0 (26.7)
NTIS score, mean (SD)	*n* = 78 6.2 (2.1)	*n* = 158 6.8 (2.0)	*n* = 155 6.8 (1.9)	*n* = 391 6.7 (2.0)

AD atopic dermatitis, *%BSA* percentage of body surface area, *CDLQI* Children's Dermatology Life Quality Index, *DLQI* Dermatology Life Quality Index, *EASI* Eczema Area and Severity Index, *EQ-5D-5L* EuroQol 5-Dimension 5-Level Scale, *EQ-5D-Y* EuroQol 5-Dimension Youth Scale, *HADS* Hospital Anxiety and Depression Scale, *IGA* Investigator's Global Assessment, *OTC* over-the-counter, *POEM* Patient-Oriented Eczema Measure, *Pruritus-NRS*, Pruritus Numerical Rating Scale, *PP-NRS* Peak Pruritus Numerical Rating Scale, *PSAAD* Pruritus and Symptoms Assessment for Atopic Dermatitis, *PtGA* Patient Global Assessment, *SD* standard deviation, *WPAI-AD* Work Productivity and Activity Impairment Questionnaire–Atopic Dermatitis, Version 2.0

[a]For patients aged ≥ 18 years

[b]For patients aged < 18 years

[c]Only patients who were employed completed work-related items

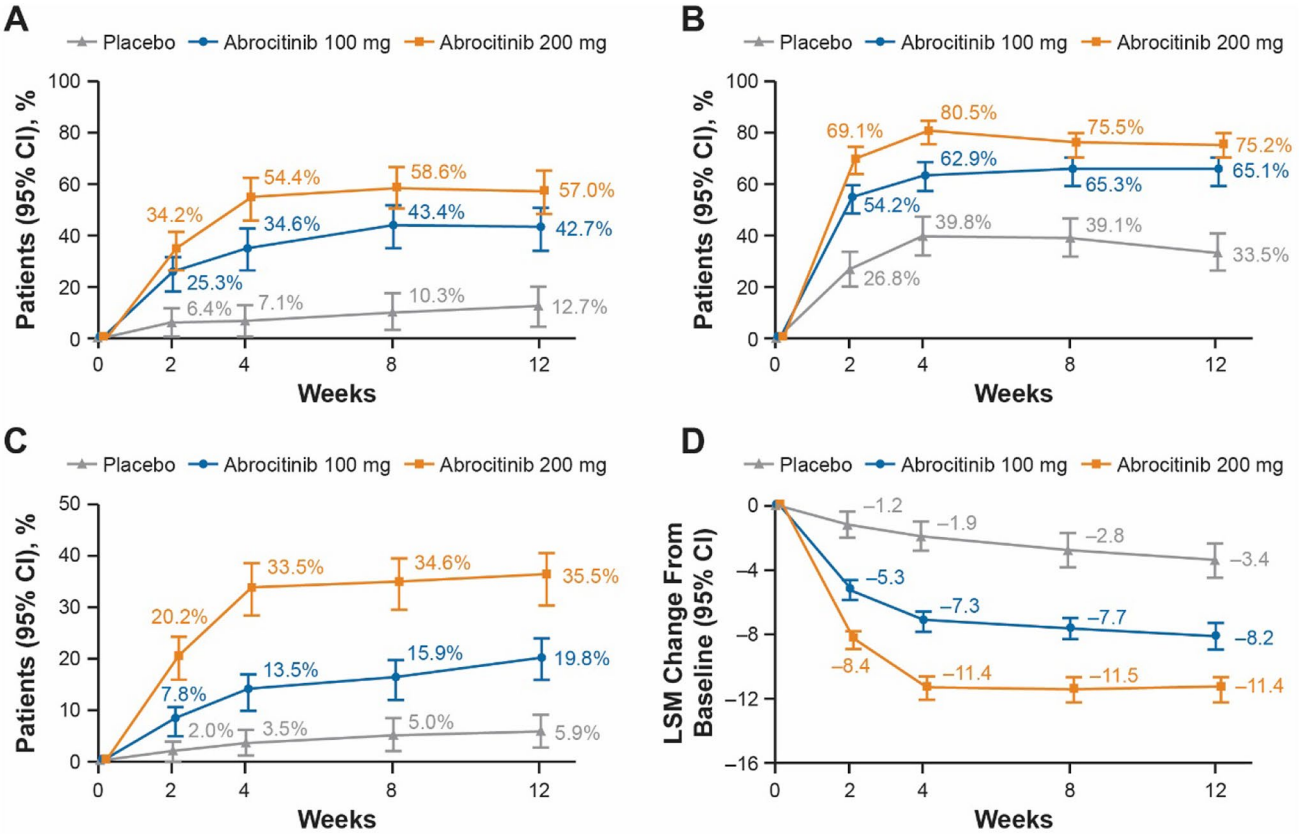

Fig. 1 Proportion of patients with **a** a ≥ 4-point improvement in the Night Time Itch Scale (NTIS) score, **b** a 1-point improvement[a] in the Pruritus and Symptoms Assessment for Atopic Dermatitis (PSAAD) total score, **c** Patient Global Assessment (PtGA) of clear or almost clear with a ≥ 2-point improvement, and **d** a change from baseline in the Patient-Oriented Eczema Measure (POEM) total score. *CI* confidence interval, *LSM* least-squares mean. [a]≥ 1-point improvement is the clinically important response for the PSAAD total score

3.3 Depression, Anxiety, and Fatigue

Mean HADS depression subscale scores (200 mg, 100 mg, and placebo) were 4.2 (3.8), 4.3 (4.0), and 4.5 (3.6) at baseline and 2.4 (3.0), 2.7 (3.2), and 4.0 (3.9) at week 12, respectively. Mean HADS anxiety subscale scores (200 mg, 100 mg, and placebo) were 5.8 (4.0), 6.0 (4.3), and 6.6 (4.0) at baseline and 3.8 (3.7), 4.1 (3.7), and 4.9 (4.0) at week 12, respectively.

Decreases from baseline in HADS depression and anxiety subscale scores were greater for abrocitinib-treated patients at all time points (Fig. 2). Among adults with baseline HADS depression score ≥ 8, 32 of 53 patients (60.4%), 28 of 60 patients (46.7%), and 9 of 33 patients (27.3%) in the 200-mg, 100-mg, and placebo groups, respectively, achieved HADS depression scores < 8 at week 12. Among adults with baseline HADS anxiety scores ≥ 8, 53 of 98 patients (54.1%), 48 of 100 patients (48.0%), and 17 of 67 patients (25.4%) in the 200-mg, 100-mg, and placebo groups, respectively, achieved HADS anxiety score < 8 at week 12.

Mean FACIT-F scores (200 mg, 100 mg, and placebo) were 38.3 (10.6), 37.4 (11.8), and 37.9 (10.2) at baseline and 41.9 (8.9), 40.6 (10.4), and 37.4 (12.1) at week 12, respectively. For adult patients, the least-squares mean change (95% CI) from baseline to week 12 in FACIT-F scores was 3.9 (2.9–4.9) in the abrocitinib 200-mg group and 2.9 (1.9–3.9) in the abrocitinib 100-mg group compared with 0.6 (–2.2 to 0.9) in the placebo group. In adolescent patients, mean Peds-FACIT-F scores (200 mg, 100 mg, and placebo) were 37.1 (7.7), 36.2 (9.0), and 35.8 (7.8) at baseline and 39.8 (6.4), 37.9 (9.0), and 37.7 (7.9) at week 12. Least-squares mean change (95% CI) from baseline to week 12 in Peds-FACIT-F was 3.0 (1.3–4.7) in the abrocitinib 200-mg group and 1.4 (– 0.3 to 3.1) in the abrocitinib 100-mg group vs 1.5 (– 1.1 to 4.0) in the placebo group. Among patients with FACIT-F/Peds-FACIT-F ≥ 30 at baseline (i.e., severe fatigue; $n = 224$ for abrocitinib 200 mg, $n = 209$ for abrocitinib 100 mg, $n = 93$ for placebo), 10 (4.5%), 14 (6.7%), and 13 (14.0%), respectively, achieved FACIT-F/Peds-FACIT-F < 30 at week 12.

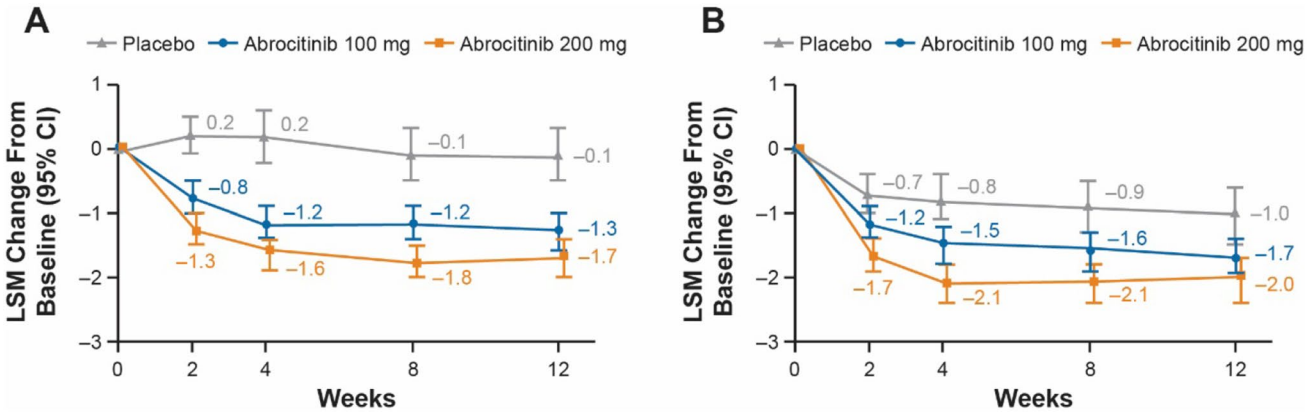

Fig. 2 Change in Hospital Anxiety and Depression Scale (HADS) **a** depression and **b** anxiety subscale scores. *CI* confidence interval, *LSM* least-squares mean

3.4 QoL and Productivity Impact

Mean EQ-5D-5L index scores (200 mg, 100 mg, and placebo) were 0.80 (0.14), 0.79 (0.15), and 0.78 (0.15) at baseline and 0.9 (0.1), 0.9 (0.1), and 0.8 (0.2) at week 12, respectively. For adult patients, both abrocitinib doses improved EQ-5D-5L index scores compared with placebo (Fig. 3a). Mean EQ-5D-Y index scores (200 mg, 100 mg, and placebo) were 0.65 (0.32), 0.66 (0.36), and 0.63 (0.39) at baseline and 0.9 (0.2), 0.8 (0.3), and 0.8 (0.3) at week 12, respectively. For adolescents, abrocitinib 200 mg improved EQ-5D-Y index scores compared with placebo (Fig. 3b).

Mean SF-36v2 mental component summary scores (200 mg, 100 mg, and placebo) were 47.9 (10.7), 48.3 (10.8), and 48.6 (9.2) at baseline and 51.5 (9.4), 50.3 (10.3), and 48.8 (9.7) at week 12, respectively. Mean SF-36v2 physical component summary scores (200 mg, 100 mg, and placebo) were 46.0 (8.0), 45.2 (9.0), and 46.0 (8.1) at baseline and 51.0 (7.5), 49.6 (7.6), and 46.8 (8.4) at week 12, respectively. Improvements from baseline to week 12 in SF-36v2 mental and physical component summary scores as well as all eight domain scores were greater for abrocitinib 200 mg and 100 mg than for placebo (Fig. 3c). Mean DLQI total scores (200 mg, 100 mg, and placebo) were 14.4 (6.6), 15.1 (7.1), and 14.3 (7.2) at baseline and 4.9 (5.6), 6.9 (6.2), and 10.3 (7.9) at week 12, respectively. By week 12, abrocitinib-treated patients reported a greater shift in DLQI/CDLQI band descriptors toward no or a small impact on disease-specific QoL than placebo-treated patients (Fig. 4). Adult patients treated with abrocitinib 200 mg or 100 mg experienced improvement in all individual items of DLQI (effect on symptom severity, embarrassment or self-consciousness, daily activities, clothing, social/leisure activities, performance of sports, prevention of work/study, impairment of work/study, personal relationships, sex life, and burden of treatment) compared with patients treated with placebo from weeks 2 to 12 (Fig. 1 of the ESM). In adolescent patients, mean CDLQI total scores (200 mg, 100 mg, and placebo) were 13.1 (5.5), 12.4 (6.4), and 12.5 (6.3) at baseline and 4.3 (3.8), 6.4 (5.2), and 9.6 (5.2) at week 12, respectively. Adolescent patients treated with abrocitinib 200 mg or 100 mg experienced improvement in the individual items on CDLQI that address effects on symptom severity, embarrassment or self-consciousness, sleep, and burden of treatment compared with patients treated with placebo from weeks 2 to 12 (Fig. 2 of the ESM). Mean percentages of activity impairment measured by WPAI-AD (200 mg, 100 mg, and placebo) were 43.0 (25.6), 41.0 (27.5), and 41.9 (27.2) at baseline and 20.5 (25.3), 22.7 (25.2), and 38.0 (28.6) at week 12, respectively. Employed abrocitinib-treated patients reported greater reductions from baseline to week 12 in the percentage of impairment while working and the percentage of overall work impairment compared with placebo-treated patients (Table 4). Likewise, abrocitinib-treated patients reported greater reductions in activity impairment from baseline to week 12 than placebo-treated patients (Table 4).

4 Discussion

This pooled analysis from three placebo-controlled studies showed that adults and adolescents with moderate-to-severe AD treated once daily with oral abrocitinib 200 mg or 100 mg monotherapy experienced clinically meaningful improvements in all domains of patient-reported disease-specific symptoms and HRQoL that were observed starting at the first post-baseline assessment (week 2) and sustained over a period of 12 weeks. These improvements were observed across a global measure (PtGA), single-symptom measures (Pruritus-NRS/PP-NRS, NTIS), and multi-item measures that included assessments of sleep disturbance, itch, skin pain, erythema, and other skin signs of AD

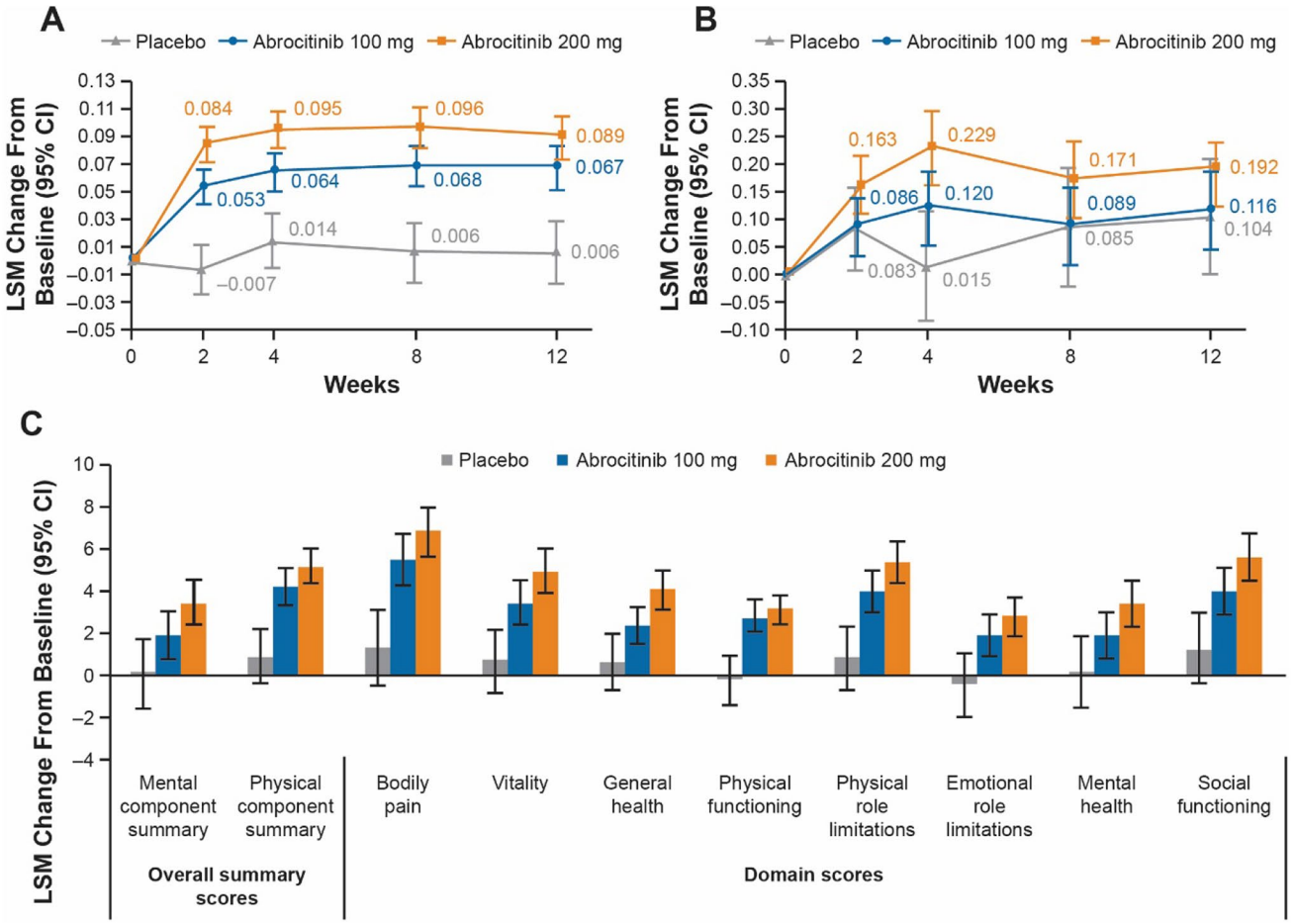

Fig. 3 Change from baseline in **a** the EuroQol 5-Dimension 5-Level Scale (EQ 5D-5L) index score, [a]**b** EuroQol 5-Dimension Youth Scale (EQ 5D-Y) index scores,[b] and **c** Short Form-36 Health Survey, Version 2, Acute (SF-36v2) scores at week 12. *CI* confidence interval, *LSM* least-squares mean. [a]For patients ≥ 18 years of age. [b]For patients < 18 years of age

(POEM, PSAAD). These improvements are supported by reduced depression, anxiety, and fatigue (HADS, FACIT-F, Peds-FACIT-F) as well as improved disease-specific (DLQI, CDLQI) and general HRQoL (EQ-5D-5L, EQ-5D-Y, SF-36v2) and improved work and general productivity among employed patients (WPAI-AD). The data generally show that abrocitinib treatment resulted in dose-dependent improvements, showing that a higher dose of abrocitinib is associated with greater improvements in PROs and HRQoL assessments, and greater proportions of patients benefit from the treatment in these outcomes. These results are consistent with previously reported trends in clinical efficacy outcomes in the individual studies included in this analysis and a pooled analysis of abrocitinib monotherapy studies focusing on itch relief [19–21, 48]. Finally, the changes from baseline reported in this study (POEM, EQ-5D-5L, and SF-36v2) were above meaningful changes previously reported in the literature [42, 49, 50].

Starting at the first post-baseline assessment (week 2) and increasing to week 12, substantially greater proportions of patients treated with abrocitinib reported clear or almost clear skin via PtGA compared with placebo. Although the baseline disease severity in the total population differed by clinician (IGA) and patient (PtGA) assessment, the trend in improvement in disease severity was consistent with both assessments by week 12. Likewise, substantially greater proportions of abrocitinib-treated patients than placebo-treated patients reported "no impact" on QoL (DLQI/CDLQI band descriptors) at weeks 4 and 12, suggesting both abrocitinib doses improved disease-specific QoL compared with placebo. These improvements in having little-to-no disease activity and impact are especially notable given the severity of disease and impairment observed at baseline in this population.

A recent systematic review and network meta-analysis (which included only the phase IIb study data for

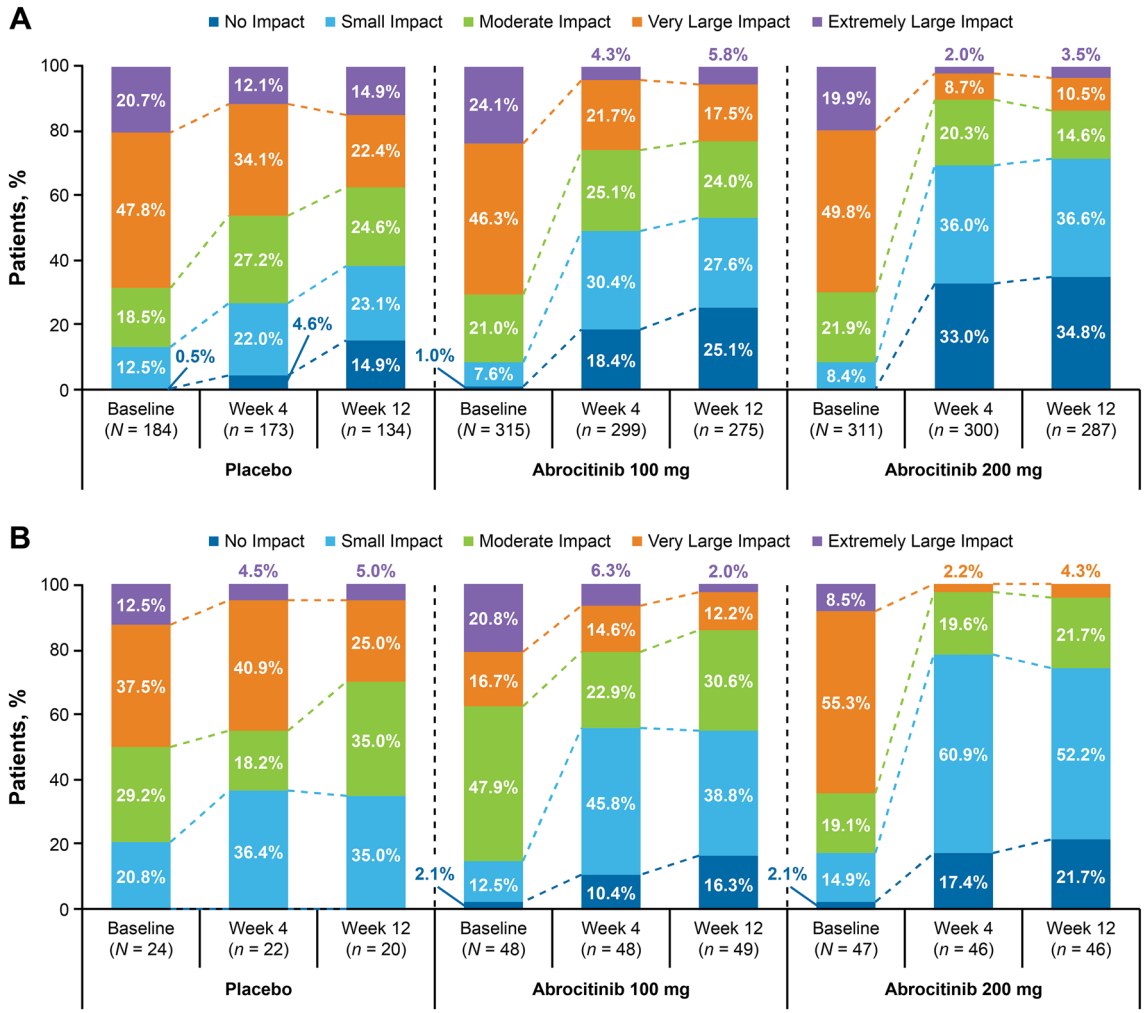

Fig. 4 Impact of treatment on **a** Dermatology Life Quality Index (DLQI)[a] and **b** Children's Dermatology Life Quality Index (CDLQI)[b] band descriptors. [a]For patients ≥ 8 years of age. [b]For patients < 18 years of age

Table 4 Change from baseline in WPAI-AD scores at week 12

LSM change (95% CI)	Placebo ($N = 210$)	Abrocitinib	
		100 mg ($N = 369$)	200 mg ($N = 363$)
Percentage work time missed[a]	$n = 42$ − 1.7 (− 7.0 to 3.5)	$n = 93$ − 0.1 (− 3.3 to 3.0)	$n = 79$ − 2.7 (− 6.2 to 0.8)
Percentage impairment while working[a]	$n = 42$ − 4.7 (− 12.4 to 2.9)	$n = 92$ − 18.5 (−23.2 to − 13.9)*	$n = 76$ − 22.7 (−27.8 to − 17.5)**
Percentage overall work impairment[a]	$n = 42$ − 5.0 (− 12.8 to 2.8)	$n = 92$ −18.7 (−23.4 to − 14.0)*	$n = 76$ − 22.9 (−28.2 to − 17.6)**
Percentage activity impairment	$n = 70$ − 3.3 (− 9.8 to 3.3)	$n = 139$ − 19.4 (− 23.5 to − 15.2)**	$n = 138$ − 21.5 (− 25.6 to − 17.4)***

WPAI-AD included in JADE MONO-2 only

CI confidence interval, *LSM* least-squares mean, *WPAI-AD* Work Productivity and Activity Impairment Questionnaire–Atopic Dermatitis, Version 2.0, *$p < 0.05$; **$p < 0.001$; ***$p < 0.0001$ vs placebo

[a]Only patients who were employed completed work-related items

abrocitinib) found that improvements in Pruritus-NRS/PP-NRS, POEM, and DLQI scores for abrocitinib 200 mg were comparable to those observed for dupilumab [51]. The majority of improvement in itch with abrocitinib (proportion of patients achieving PP-NRS4 and PP-NRS score changes from baseline) was observed within the first 2 weeks of treatment [48]. In the context of other systemic treatments with more gradual improvements in itch (i.e., the majority of itch relief with dupilumab is observed over the first 4 weeks of treatment [52]), the short time to maximal itch relief with abrocitinib treatment is particularly beneficial to patients, especially during acute flares. The more rapid onset of itch relief with abrocitinib vs dupilumab has also been confirmed in JADE COMPARE, which compared short-term efficacy and safety data between abrocitinib and dupilumab treatments in patients with moderate-to-severe AD [53]. Other JAK inhibitors, such as baricitinib, have also shown a rapid and sustained itch relief [54]; however, because different itch metrics were used, comparing abrocitinib to baricitinib in the onset of itch relief is challenging. Immediate and sustained relief from itch has been identified as the most relevant benefit expected from new treatments based on a survey of individuals with eczema [25]. This rapid onset of itch relief is also reflected in early separation of abrocitinib from placebo in other measures of AD symptoms, psychological burden, and QoL.

As with any post hoc analysis, the strength of these results may be limited. It is possible that improvements in itch could have led to improvements in sleep, hence decreasing fatigue and increasing productivity. Future studies will need to address the interdependency of itch and sleep improvement with QoL outcomes. The PRO instruments were administered at specific time points, influencing the time to detection of an improvement. In addition, differences in PRO instruments across studies resulted in smaller data sets for some of the endpoints. The exclusion of patients with suicidal ideation/behaviors or other psychiatric disorders from the phase III studies may limit the generalizability of these results to patients with depressive symptoms, which affect up to 20% of patients with AD (compared with ~15% of patients without AD) [55]. Last, these studies were relatively short (12 weeks); the long-term efficacy and safety of abrocitinib are being assessed in ongoing trials.

5 Conclusions

The results of these analyses suggest that abrocitinib is effective for adult and adolescents with moderate-to-severe AD [19, 21]. These results of PRO assessments provide important information on the efficacy of abrocitinib from the patient perspective and complement clinician-reported efficacy and safety outcomes.

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Declarations

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Conflict of Interest Jonathan I. Silverberg has served as an investigator for Celgene, Eli Lilly, F. Hoffmann-LaRoche, Menlo Therapeutics, Realm Therapeutics, Regeneron, and Sanofi; as a consultant for Pfizer Inc., AbbVie, Anacor, AnaptysBio, Arena Pharmaceuticals, Dermira, Dermavant, Eli Lilly, Galderma, GSK, Glenmark, Incyte, Kiniksa, LEO Pharma, Menlo Therapeutics, Novartis, Realm Therapeutics, Regeneron, and Sanofi; and as a speaker for Regeneron and Sanofi. Jacob P. Thyssen is an advisor/investigator or speaker for Pfizer, AbbVie, Eli Lilly, LEO Pharma, Regeneron, and Sanofi-Genzyme. Eric L. Simpson is a consultant for Pfizer, AbbVie, Celgene, Eli Lilly, Galderma, GlaxoSmithKline, Menlo Therapeutics, LEO Pharma, and Regeneron and a principal investigator for AbbVie, GlaxoSmithKline, LEO Pharma, Novartis, Regeneron, Tioga Pharmaceuticals, and Vanda Pharmaceuticals. Gil Yosipovitch has been a consultant and advisor for Bellus, Pfizer, Eli Lilly, Galderma, LEO Pharma, Kiniksa Pharmaceuticals, Menlo Therapeutics, Novartis, Sanofi-Regeneron, and Trevi Therapeutics, and a principal investigator for Pfizer, Galderma, Kiniksa Pharmaceuticals, LEO Pharma, Sanofi-Regeneron, Novartis, and Sun Pharmaceutical Industries. Sonja Ständer is a consultant and/member of advisory boards for Pfizer Inc., Almirall, Bayer, Beiersdorf, Bellus Health, Bionorica, Cara Therapeutics, Celgene, Clexio, DS Biopharma, Galderma, Menlo Therapeutics, Novartis, Nuformix, Perrigo, Sanofi, Sienna Biopharmaceutical, Trevi Therapeutics, and Vifor Pharma; has received research grants from the German Research Foundation (DFG), the European Academy of Dermatology and Venereology (EADV), Almirall, Beiersdorf, Galderma, LEO Pharma, Kiniksa Pharmaceuticals, Menlo Therapeutics, Novartis, Sanofi, and Trevi Therapeutics; and has been an investigator for Dermasence, Galderma, Kiniksa Pharmaceuticals, Menlo Therapeutics, Novartis, Sanofi, Trevi Therapeutics, and Vanda Pharmaceuticals. Hernan Valdez, Ricardo Rojo, Pinaki Biswas, Daniela E. Myers, Claire Feeney, and Marco DiBonaventura are employees and shareholders of Pfizer Inc.

Ethics Approval The institutional review board at each study site approved the study protocol and written informed consent was provided by parents/legal guardians. The study was conducted in accordance with the protocol, local legal and regulatory requirements, and the general principles set forth in the International Ethical Guidelines for Biomedical Research Involving Human Subjects, International Conference on Harmonisation Guideline for Good Clinical Practice, and the Declaration of Helsinki.

Consent to Participate Written informed consent was provided by the participants of all studies.

Availability of Data and Material Upon request, and subject to certain criteria, conditions, and exceptions (see https://www.pfizer.com/science/clinical-trials/trial-data-and-results for more information), Pfizer will provide access to individual de-identified participant data from

Pfizer-sponsored global interventional clinical studies conducted for medicines, vaccines, and medical devices (1) for indications that have been approved in the USA and/or the European Union or (2) in programs that have been terminated (i.e., development for all indications has been discontinued). Pfizer will also consider requests for the protocol, data dictionary, and statistical analysis plan. Data may be requested from Pfizer trials 24 months after study completion. The de-identified participant data will be made available to researchers whose proposals meet the research criteria and other conditions, and for which an exception does not apply, via a secure portal. To gain access, data requestors must enter into a data access agreement with Pfizer.

Author Contributions All authors contributed to the design of the study; participated in the acquisition, analysis, and/or interpretation of data; reviewed and critically revised the report for important intellectual content; and gave final approval of the version that was submitted.

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