ORIGINAL ARTICLE

High threshold efficacy responses in moderate-to-severe atopic dermatitis are associated with additional quality of life benefits: pooled analyses of abrocitinib monotherapy studies in adults and adolescents

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Abstract

Background Once-daily abrocitinib treatment provided meaningful improvements in signs and symptoms of moderate-to-severe atopic dermatitis (AD) in randomized controlled studies.

Objective To evaluate proportions of patients with responses meeting higher threshold efficacy responses than commonly used efficacy end points and to determine if these responses were associated with quality-of-life (QoL) benefits.

Methods Data from a phase 2b (NCT02780167) and two phase 3 studies (NCT03349060/JADE MONO-1; NCT03575871/JADE MONO-2) in adult and adolescent patients (N = 942) with moderate-to-severe AD receiving once-daily abrocitinib 200 mg, abrocitinib 100 mg or placebo were pooled. Commonly used (Eczema Area and Severity Index [EASI]-75 and ≥4-point improvement in Pruritus Numerical Rating Scale [PP-NRS4]) and higher threshold efficacy end points (EASI-90 to <EASI-100, EASI-100 or PP-NRS0/1 response) were evaluated. Proportions of patients across Children's Dermatology Life Quality Index/Dermatology Life Quality Index (CDLQI/DLQI) band descriptors who achieved various efficacy end points were analysed.

Results More abrocitinib-treated patients achieved commonly used or higher threshold efficacy end points at week 12 vs. placebo. More abrocitinib-treated patients who achieved higher threshold efficacy end points reported 'no effect' of AD on QoL (by CDLQI/DLQI) at week 12 vs. those who achieved commonly used but not higher threshold efficacy end points (PP-NRS0/1 vs. PP-NRS4 but not PP-NRS0/1 responders [200 mg: 66.3% vs. 17.5%; 100 mg: 62.1% vs. 20.0%]; EASI-100, EASI-90 to <EASI-100 vs. EASI-75 to <EASI-90 responders [200 mg: 67.6%, 48.9% vs. 28.8%; 100 mg: 63.2%, 48.1% vs. 36.7%]).

Conclusions Substantial proportions of patients with moderate-to-severe AD receiving abrocitinib met higher threshold efficacy end points, and this was associated with meaningful additional QoL benefits compared with those who did not meet these higher efficacy thresholds. Not only do a substantial proportion of abrocitinib-treated patients achieve higher threshold efficacy end points but they also do so in a similar timeframe as the more commonly used thresholds for efficacy end points.

Clinical trials NCT02780167, NCT03349060 and NCT03575871.

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Conflicts of interest

SS is an investigator for Dermasence, Galderma, Kiniksa, Menlo Therapeutics, Novartis, Trevi Therapeutics, Sanofi and Vanda; a member of scientific advisory boards for Beiersdorf, Celgene, Galderma, Kiniksa, Menlo Therapeutics, Sienna Biopharmaceuticals and Trevi Therapeutics; and a consultant for AbbVie, Almirall, BELLUS Health, Bionorica, Cara

The patients in this manuscript have given written informed consent to publication of their case details.

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Introduction

Atopic dermatitis (AD) is a chronic, relapsing, inflammatory skin condition characterized by pruritus, eczematous lesions and dry skin that affects up to 25% of children and 5% to 10% of adults worldwide.[1–7] The signs and symptoms of AD, especially pruritus, are severely burdensome and can lead to the development of depressive symptoms,[8–10] psychological distress and sleep disturbance,[10–13] which impact patient quality of life (QoL).[10,14–16] Abrocitinib, an oral, once-daily, Janus kinase 1 (JAK1) inhibitor, was recently approved for the treatment of moderate-to-severe AD in adults and adolescents in Great Britain[17] and Japan[18] and in adults in the European Union[19] and the United States.[20] Inhibition of JAK1 modulates various cytokines relevant to the pathophysiology of AD, including interleukin (IL)-4, IL-13, IL-31 and thymic stromal lymphopoietin (TSLP).[21–23] Additionally, inhibition of the JAK1 pathway ameliorates the sensation of pruritus through direct neuronal JAK1 inhibition.[24] Hence, selective inhibition of JAK1 modulates multiple downstream signalling pathways critical to the pathogenesis and symptoms of AD.

Abrocitinib monotherapy was effective and well tolerated in clinical studies in patients with moderate-to-severe AD.[25–27] In JADE MONO-1 and JADE MONO-2, identical phase 3 studies in adult and adolescent patients with moderate-to-severe AD, significantly greater proportions of patients treated with abrocitinib (200 mg or 100 mg) achieved commonly used efficacy threshold responses defined as Investigator Global Assessment (IGA) 0/1 response (clear [0] or almost clear [1] with ≥2-grade improvement), ≥75% improvement in Eczema Area and Severity Index score (EASI-75) response and/or ≥4-point improvement from baseline in Peak Pruritus Numerical rating scale (PP-NRS4) response compared with patients treated with placebo, and with a manageable safety profile.[26,27] Among the responders fulfilling these commonly used efficacy thresholds, a subset met higher threshold efficacy responses; for example, among those reaching EASI-75 response, some had attained EASI-90 or EASI-100, and among those reaching PP-NRS4 response, some achieved PP-NRS0/1 (the latter reflecting profound itch control). Attaining these higher threshold efficacy responses may be associated with additional, clinically meaningful improvement in QoL. The objectives of these *post hoc* analyses were to determine the proportion of patients in the phase 2b and phase 3 abrocitinib monotherapy trials, who achieved higher threshold efficacy end points (90% improvement in EASI to <100% improvement in EASI [EASI-90 to <EASI-100 response], EASI-100 and PP-NRS0/1), if the time to onset of these higher efficacy threshold responses differed from that observed for commonly used efficacy end points (EASI-75 and PP-NRS4), and to determine if these higher threshold efficacy responses were associated with additional and clinically meaningful improvement in QoL vs. commonly used efficacy responses.

Methods

Study design

These analyses used data pooled from three similarly designed abrocitinib monotherapy trials, including a phase 2b trial (NCT02780167) and two phase 3 trials (NCT03349060, JADE MONO-1; NCT03575871, JADE MONO-2) in adult and adolescent patients with moderate-to-severe AD treated with once-daily abrocitinib 200 mg, abrocitinib 100 mg or placebo.[25–27] Patients were randomly assigned in a 1:1:1:1:1 ratio

in the phase 2b study to receive abrocitinib (200 mg, 100 mg, 30 mg or 10 mg) or placebo and in a 2:2:1 ratio in the phase 3 studies to receive abrocitinib (200 mg or 100 mg) or placebo. Details of all three studies along with primary efficacy and safety results were previously reported.[25–27] All study documents and procedures were approved by the appropriate institutional review board/ethics committee at each study site. The studies were conducted in compliance with the ethical principles originating in or derived from the Declaration of Helsinki and in compliance with all International Council for Harmonisation Good Clinical Practice Guidelines. All local regulatory requirements were followed. An internal review committee monitored the safety of patients throughout the studies. All patients provided written informed consent.

Patients

Study participants were patients aged 18–75 years (phase 2b) or ≥ 12 years (phase 3) with a clinical diagnosis of moderate-to-severe AD (IGA ≥3, EASI ≥12 [phase 2b] or ≥ 16 [phase 3], percentage of body surface area involvement [%BSA] ≥10, PP-NRS; [used with permission of Regeneron Pharmaceuticals, Inc., and Sanofi[28]] ≥4 [phase 3 only]), for ≥1 year (phase 2b) and recent (phase 3: within 6 months) history of inadequate response to topical medications (corticosteroids or calcineurin inhibitors) given for ≥4 weeks or an inability to receive topical treatment because it was medically inadvisable. Previous dupilumab use was permitted in the phase 3 studies if it had been >6 weeks before study initiation.[26,27] Patients who previously used JAK inhibitors within 12 weeks (phase 2b) or ever (phase 3) or oral immunosuppressant agents (i.e. cyclosporine, azathioprine, methotrexate, mycophenolate mofetil and systemic corticosteroids) within 4 weeks or five half-lives (whichever was longer) were excluded from the studies.[25–27] Rescue medication (including topical corticosteroids) was prohibited during the studies. Full inclusion and exclusion criteria are published elsewhere.[25–27]

Post hoc analysis end points

End points assessed in this *post hoc* analysis included: proportion of patients who achieved commonly used efficacy end points and the proportion of patients who achieved higher threshold efficacy end points (EASI-90 to <EASI-100 response, EASI-100 response or PP-NRS score of 0 or 1 [i.e. baseline score ≥2 achieving score <2; PP-NRS0/1 response]) from baseline to week 12. Median time to response in patients with EASI-100 response, EASI-90 to <EASI-100 response (defined as % improvement in EASI ≥90% to <100%), EASI-75 to <EASI-90 response (defined as % improvement in EASI ≥75% to <90%), PP-NRS0/1 response and PP-NRS4 but not PP-NRS0/1 response was also analysed. In addition, separate analyses evaluating the association of these end points with QoL improvement at week 12 were conducted. QoL improvement was stratified by (Children's) Dermatology Life Quality Index (CDLQI/DLQI) severity bands, which describe the magnitude of the negative impact on QoL. CDLQI/DLQI scores of 0–1 corresponded to 'no effect', scores of 2–5 to 'small effect', scores of 6–10 to 'moderate effect', scores of 11–20 to 'very large effect' and scores of 21–30 to 'extremely large effect'.[29]

Statistical analyses

Binary end points were analysed using the Cochran–Mantel–Haenszel test, adjusted by randomization strata. Patients who permanently discontinued the study were defined as non-responders at all visits after the last observation. Continuous end points were analysed using a mixed-effect model with repeated measures based on all observed data. The model included factors for treatment group, randomization strata, visit, treatment-by-visit interaction, and relevant baseline value. Median times to response were analysed with observed responses (not including patients with missing or censored response data) using empirical methods for confidence intervals (CIs) for quantiles. These analyses were not controlled for multiplicity and no statistical hypotheses were tested.

Results

Patients

Demographics and baseline characteristics were similar among pooled monotherapy patients treated with abrocitinib or placebo (Table 1). Mean (standard deviation) baseline EASI, PP-NRS, DLQI and CDLQI scores were 28.8 (12.7), 7.0 (1.9), 14.6 (6.9) and 12.7 (6.0) respectively. These baseline values indicate moderate-to-severe AD at baseline, and that the disease had a 'very large effect' on QoL.

Depth of response to abrocitinib

In the pooled analysis, patients treated with abrocitinib had marked improvement in EASI scores compared with placebo. At week 12, the proportions of patients (95% CI) who achieved EASI-75 response were 62.3% (57.2–67.3), 41.9% (36.9–47.0) and 12.2% (7.7–16.7) for the abrocitinib 200 mg, abrocitinib 100 mg and placebo groups respectively (Fig. 1). At week 12, greater proportions of patients treated with abrocitinib achieved EASI-75 to <EASI-90 response (22.3% [17.9–26.6], 20.0% [15.9–24.1] and 6.3% [3.0–9.7]) than patients treated with placebo (Fig. 1). Similar trends were found at higher thresholds for EASI response. At week 12, greater proportions of abrocitinib-treated patients achieved EASI-90 to <EASI-100 (29.3% [24.6–34.0], 15.9% [12.1–19.6] and 5.9% [2.6–9.1]) (Fig. 1) and EASI-100 response (10.7% [7.5–13.9], 6.0% [3.6–8.5] and 0% [0–1.8]) compared with placebo for the abrocitinib 200 mg, 100 mg and placebo groups respectively (Fig. 1).

Greater proportions of patients treated with abrocitinib achieved PP-NRS4 response at week 12 compared with placebo; PP-NRS4 responder proportions at week 12 were 57.3% (51.8–62.7), 42.9% (37.4–48.3) and 16.5% (11.2–21.8) for the

Table 1 Demographic and baseline characteristics

Characteristic	Pooled treatment group			
	Placebo (*n* = 210)	Abrocitinib		All (*N* = 942)
		100 mg (*n* = 369)	200 mg (*n* = 363)	
Age (years), mean (SD)	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, 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)
Black or African American	22 (10.5)	31 (8.4)	30 (8.3)	83 (8.8)
Asian	39 (18.6)	80 (21.7)	85 (23.4)	204 (21.7)
Other	3 (1.4)	2 (0.5)	5 (1.4)	10 (1.1)
Multiracial	2 (1.0)	2 (0.5)	8 (2.2)	12 (1.3)
Not reported	3 (1.4)	1 (0.3)	4 (1.1)	8 (0.8)
Ethnicity, *n* (%)				
Hispanic or Latino	11 (5.2)	14 (3.8)	12 (3.3)	37 (3.9)
Not Hispanic or Latino	196 (93.3)	352 (95.4)	349 (96.1)	897 (95.2)
Not reported	3 (1.4)	3 (0.8)	2 (0.6)	8 (0.8)
Disease duration (years), mean (SD)	23.5 (15.2)	23.7 (16.1)	22.0 (15.1)	23.0 (15.5)
EASI score (%), mean (SD)	27.6 (11.8)	29.4 (12.4)	29.0 (13.4)	28.8 (12.7)
BSA affected (%), mean (SD)	45.8 (22.1)	48.6 (22.5)	47.2 (23.6)	47.4 (22.8)
PP-NRS				
No. of patients	207	368	362	937
Mean (SD) score	7.0 (1.9)	7.1 (1.9)	7.0 (1.9)	7.0 (1.9)
DLQI[†]				
No. of patients	184	315	311	810
Mean (SD) total score	14.3 (7.2)	15.1 (7.1)	14.4 (6.6)	14.6 (6.9)
CDLQI				
No. of patients	24	48	47	119
Mean (SD) total score	12.5 (6.3)	12.4 (6.4)	13.1 (5.5)	12.7 (6.0)

[†]For patients aged 18 years or more.

AD, atopic dermatitis; BSA, body surface area; CDLQI, Children's Dermatology Life Quality Index; DLQI, Dermatology Life Quality Index; EASI, Eczema Area and Severity Index; PP-NRS, Peak Pruritus Numerical Rating Scale; SD, standard deviation.

abrocitinib 200 mg, abrocitinib 100 mg and placebo groups respectively (Fig. 2). Among PP-NRS4 responders at week 12, greater proportions of patients treated with abrocitinib achieved PP-NRS4 but not PP-NRS0/1 response (22.5% [17.8–27.2], 20.4% [15.9–24.9] and 12.6% [7.8–17.4]; Fig. 2) and the higher threshold efficacy end point of PP-NRS0/1 response (36.6% [31.3–42.0], 23.4% [18.7–28.1] and 5.3% [2.1–8.5]; Fig. 2) compared with placebo for the abrocitinib 200 mg, 100 mg and placebo groups respectively.

The efficacy of abrocitinib (200 mg and 100 mg) was better than that of placebo for all response thresholds evaluated from week 2 through week 12 (Figs. 1 and 2).

Time to response to abrocitinib

To assess the onset of observed response at the various efficacy thresholds, without overlap with higher threshold efficacy responses, analyses were performed that 'windowed' the efficacy responses for EASI-75 to <EASI-90, EASI-90 to <EASI-100, EASI-100, PP-NRS 4 but not PP-NRS0/1, and PP-NRS0/1 (Table 2).

In the pooled analysis for observed EASI-75 to <EASI-90 responders, median time to onset of response was 56 days for both abrocitinib treatment arms. For the higher threshold efficacy end point of those observed to reach EASI-90 to <EASI-100, a similar time to onset of response was observed: 56 and 58 days for abrocitinib 200 mg and abrocitinib 100 mg groups respectively. For the still higher threshold efficacy end point of EASI-100 response; however, median time to response for observed responders was greater at approximately 84 days for both abrocitinib groups.

In the pooled analysis for observed PP-NRS4 but not PP-NRS0/1 response, median time to onset was 13.5 and 29.0 days for the abrocitinib 200 mg and abrocitinib 100 mg groups

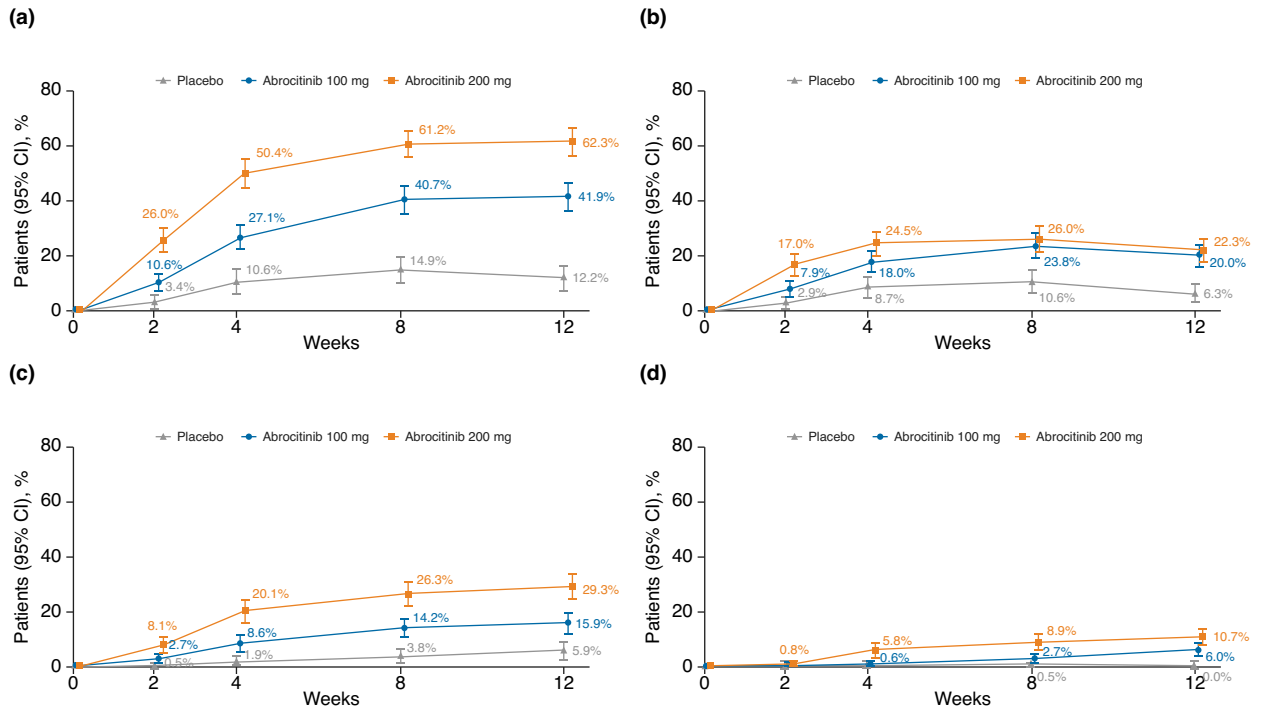


Figure 1 Proportion of patients with moderate-to-severe AD who achieved (a) EASI-75 response, (b) EASI-75 to <EASI-90 response, (c) EASI-90 to <EASI-100 response and (d) EASI-100 response at weeks 2, 4, 8 and 12. AD, atopic dermatitis; CI, confidence interval; EASI, Eczema Area and Severity Index.

respectively. For the higher threshold efficacy end point of those observed to reach PP-NRS0/1 response, median time to onset was similar at 14.5 and 29 days for the abrocitinib 200 mg and abrocitinib 100 mg groups respectively.

Relationship of quality of life with depth of response

To assess association with QoL outcomes at the various efficacy thresholds, without overlap with higher threshold efficacy responses, analyses were performed that 'windowed' the efficacy responses: EASI-75 to <EASI-90, EASI-90-to <EASI-100, EASI-100, PP-NRS4 but not PP-NRS0/1, and PP-NRS0/1 (Figs. 3 and 4).

At baseline, limited numbers of patients reported small or no effect of AD on QoL (Fig. 3a and Fig. 4a). By week 12, greater proportions of patients reported fewer effects of AD on their QoL, with the greatest benefit on QoL observed among patients experiencing higher threshold EASI and PP-NRS efficacy responses (Fig. 3b and Fig. 4b). For example, at 12 weeks, 28.8%, 36.7% and 46.2% of patients with EASI-75 to <EASI-90 for abrocitinib 200 mg, abrocitinib 100 mg and placebo, respectively, reported 'no effect' of AD on QoL, compared with 48.9%, 48.1% and 33.3% of patients with EASI-90-to <EASI-100, and with 67.6%, 63.2% and 0% in patients with EASI-100 (Fig. 3b). Thus, the proportion of patients reporting 'no effect' on their QoL by week 12 was more than double (2.34 times) among those achieving EASI-100 compared with those achieving only EASI-75 to <EASI-90.

The difference regarding QoL outcomes was even more marked between patients reaching different PP-NRS efficacy response thresholds. Approximately four times the proportion of PP-NRS0/1 responders treated with abrocitinib 200 mg (3.79 times the proportion of responders) reported that their AD had 'no effect' on their QoL at week 12, compared with PP-NRS4 responders who did not achieve PP-NRS0/1 treated with the same dose (66.3% vs. 17.5%; (Fig. 4b). Similarly, approximately three times the proportion of PP-NRS0/1 responders treated with abrocitinib 100 mg (3.11 times the proportion of responders) reported that their AD had 'no effect' on their QoL at week 12, compared with PP-NRS4 responders who did not achieve PP-NRS0/1 treated with the same dose (62.1% vs. 20.0%; Fig. 4b).

Representative patient cases

Changes in skin involvement in abrocitinib-treated patients from baseline to week 12 are shown in Fig. 5. One patient who received abrocitinib 100 mg had an EASI score of 19.8 and 3.8 at baseline and week 12, respectively, that qualified as an EASI-75 to <EASI-90 response. A second patient, who also received

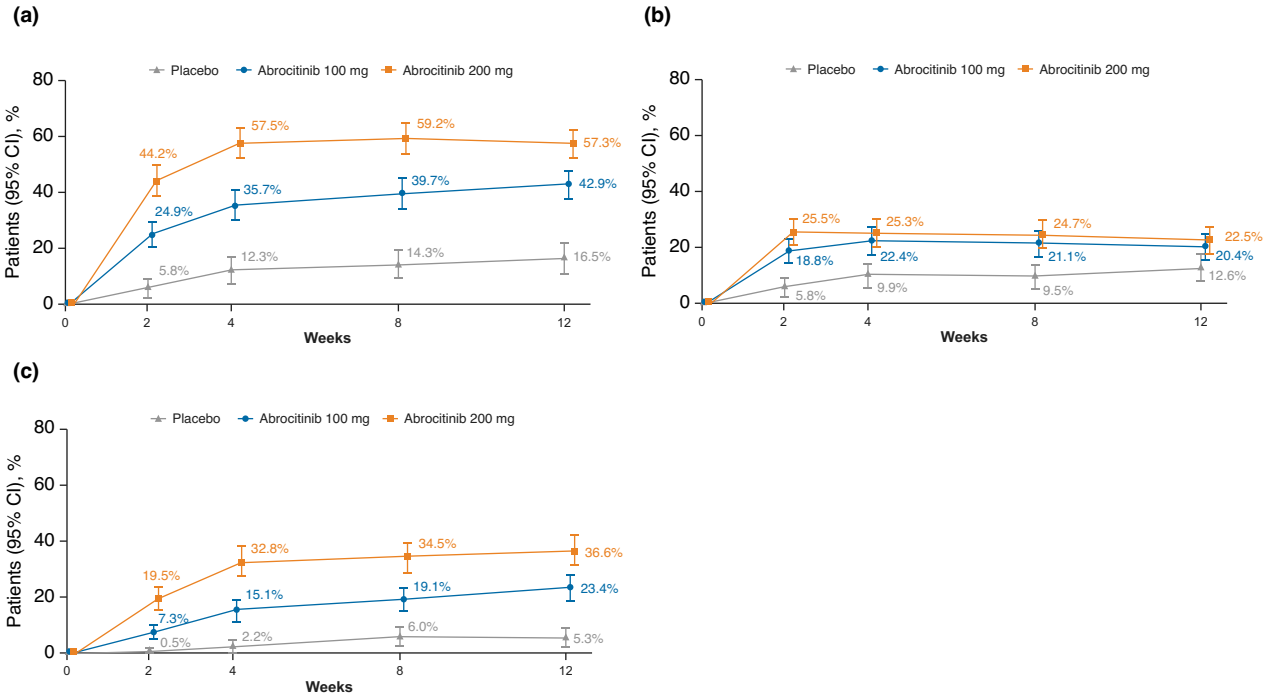


Figure 2 Proportion of patients with moderate-to-severe AD who achieved (a) PP-NRS4 response (≥4-point improvement from baseline), (b) PP-NRS4 but not PP-NRS0/1 response and (c) PP-NRS0/1 response (baseline score ≥ 2; achieving score < 2) at weeks 2, 4, 8 and 12. AD, atopic dermatitis; CI, confidence interval; PP-NRS, Peak Pruritus Numerical Rating Scale.

Table 2 Median time (days) to first response based on various efficacy end points

Days (95% CI)	Pooled treatment group		
	Placebo (*n* = 211)	Abrocitinib	
		100 mg (*n* = 370)	200 mg (*n* = 364)
EASI responses			
EASI-75	31.0 (29–57)	30.0 (29–56)	29.0 (29–29)
EASI-75 to <EASI-90	57.0 (29–85)	56.0 (30–57)	56.0 (30–57)
EASI-90	79.5 (56–85)	57.0 (56–58)	47.0 (30–57)
EASI-90 to <EASI-100	79.5 (56–85)	58.0 (56–85)	56.0 (31–57)
EASI-100	0	84.5 (57–86)	84.0 (56–85)
PP-NRS responses			
PP-NRS4	29.0 (13–58)	15.0 (11–29)	10.0 (8–12)
PP-NRS4 but not PP-NRS0/1	29.0 (10–58)	29.0 (13–57)	13.5 (9–29)
PP-NRS0/1	83.0 (11–85)	29.0 (28–56)	14.5 (12–29)

Median time to response was calculated only among subjects with an observed time of event.

abrocitinib 100 mg had an EASI score of 36.9 and 0.6 at baseline and week 12, respectively, that qualified as an EASI-90 to <EASI-100 response. A third patient who received abrocitinib 200 mg had an EASI score of 17.2 and 2.7 at baseline and week 12, respectively, that qualified as an EASI-75 to <EASI-90 response.

Discussion

The results of these *post hoc* pooled analyses indicate that substantial proportions of patients with moderate-to-severe AD achieve higher threshold efficacy end points (EASI-90 to <EASI-100, EASI-100, or PP-NRS0/1) with treatment consisting of once-daily oral abrocitinib (200 mg or 100 mg) monotherapy for 12 weeks. The median time to onset of these higher threshold efficacy responses was similar to that of the commonly used threshold efficacy end points in all treatment arms. The only exception was the highest-efficacy threshold for EASI (i.e. EASI-100), which took 1.5 times longer than the commonly used threshold efficacy end point (84 days vs. 56 days). Thus, not only do a substantial proportion of abrocitinib-treated patients achieve higher threshold efficacy end points but they do so in a similar timeframe as for more commonly used thresholds for efficacy end points. The rapid onset of higher threshold efficacy responses is an important consideration for patients as well as healthcare providers regarding the management of the signs and symptoms of AD, particularly for itch relief.

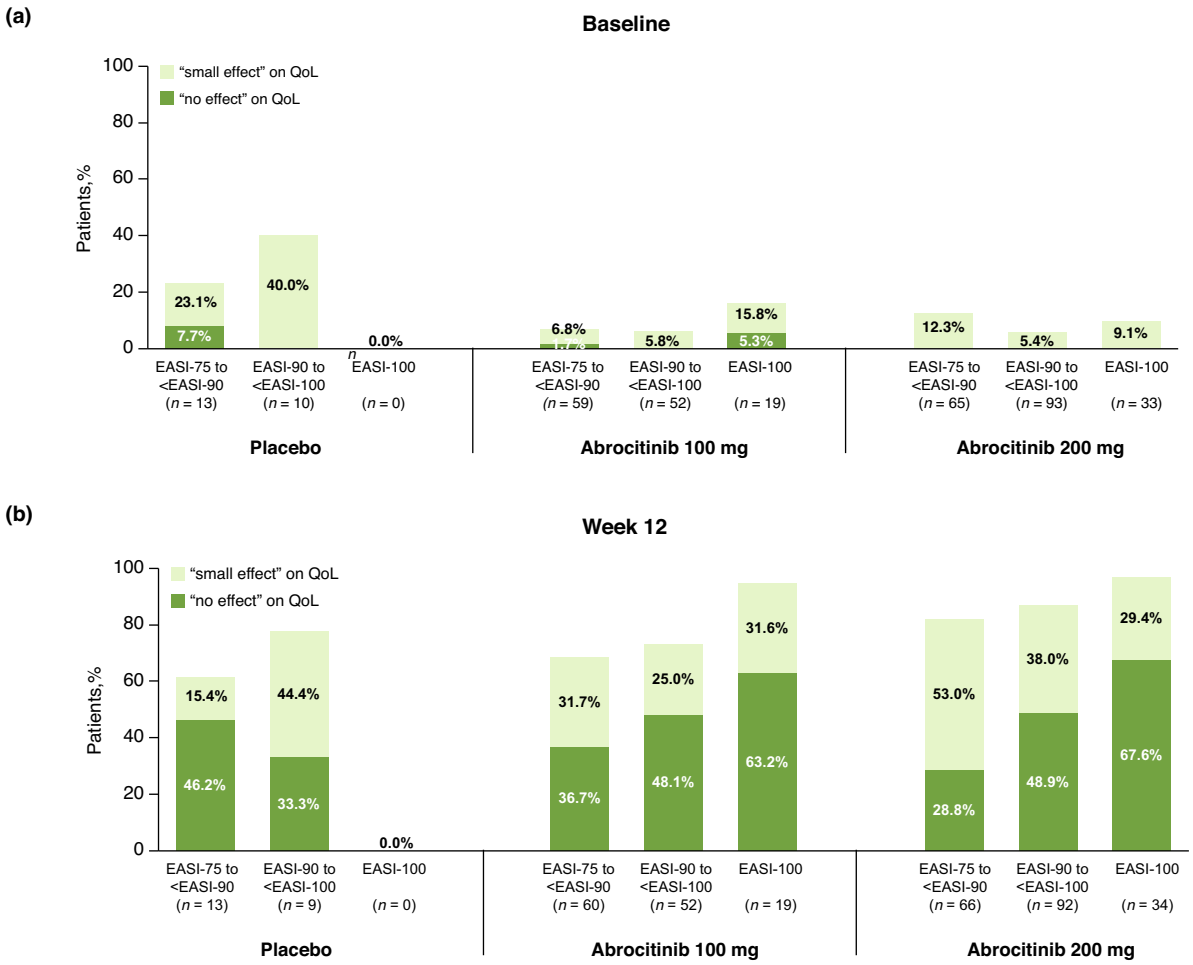


Figure 3 Distribution of CDLQI/DLQI severity bands at (a) baseline and (b) week 12 of patients with moderate-to-severe AD who achieved EASI-75 to <EASI-90 response, EASI-90 to <EASI-100 response and EASI-100 response at week 12 in the placebo, abrocitinib 100 mg and abrocitinib 200 mg treatment groups. AD, atopic dermatitis; CDLQI, Children's Dermatology Life Quality Index; DLQI, Dermatology Life Quality Index; EASI, Eczema Area and Severity Index.

Importantly, patients who met higher threshold efficacy end points reported clinically meaningful benefits to QoL compared with patients who achieved EASI-75 to <EASI-90, or PP-NRS4 but not PP-NRS0/1. Achieving higher threshold efficacy responses was associated with larger proportions of patients reporting that their AD has 'no effect' on their QoL.[30] This is of particular interest because various treatment guidelines have indicated improvement in QoL is one of the main goals of therapy.[6,31,32] Interestingly, in the small number of patients who happened to achieve high threshold efficacy responses following placebo treatment, a corresponding improvement in QoL was observed. This further supports the notable impact of attaining high threshold efficacy responses; however, they happen to be attained, on patient QoL. It is important to note, however, that high threshold efficacy responses to placebo treatment were only observed in small number of patients. The superiority of abrocitinib over placebo, both as a monotherapy and in combination with medicated topical therapies for AD, was demonstrated across a spectrum of efficacy end points in several completed, randomized, controlled, double-blind phase 3 studies.[26,27,33]

The reported improvement in QoL among patients achieving higher threshold efficacy responses may, in part, be explained by patient expectations or goals of treatment for AD. For example, patients with AD desire to achieve complete or almost complete skin clearance and report greater overall self-perceived importance of complete or almost complete skin clearance, as well as control of itch, when compared with patients with psoriasis.[30] In addition to skin clearance, itch control is also an important

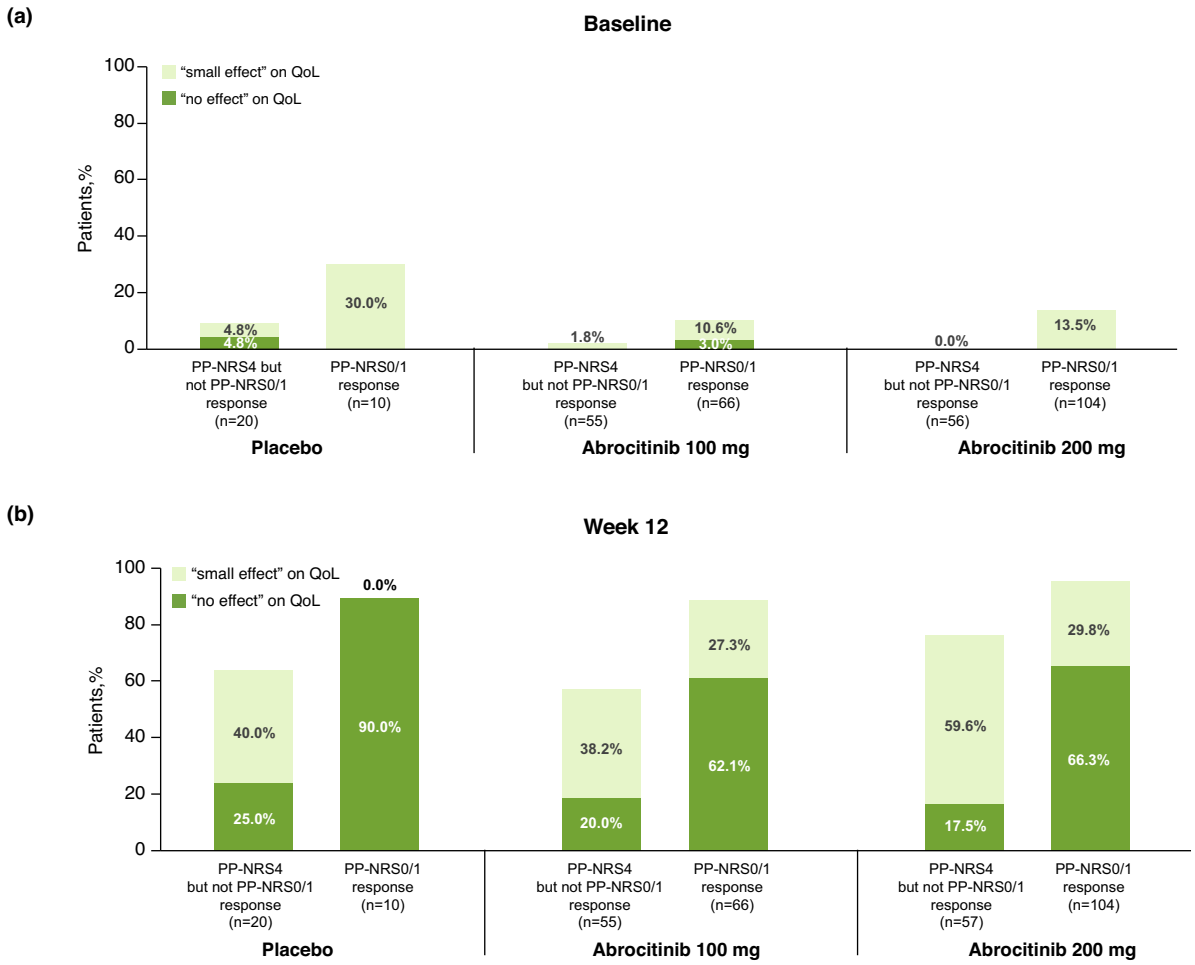


Figure 4 Distribution of CDLQI/DLQI severity bands at (a) baseline and (b) week 12 of patients with moderate-to-severe AD who achieved PP-NRS4 response but not PP-NRS0/1 response and PP-NRS0/1 response at week 12 in the placebo, abrocitinib 100 mg and abrocitinib 200 mg treatment groups. AD, atopic dermatitis; CDLQI, Children's Dermatology Life Quality Index; DLQI, Dermatology Life Quality Index; PP-NRS, Peak Pruritus Numerical Scale.

treatment aim for patients with AD.[34] Alignment on meeting patient goals that enhance the impact of therapy on QoL, especially in the context of attaining higher threshold efficacy responses in terms of skin clearance and itch, should be important considerations in guiding treatment decisions. There remains a need for better insight into the treatment targets that are important to patients, as this should affect management.

Limitations of these analyses include their *post hoc* nature, the relatively short duration of the studies (12 weeks) and that formal hypothesis testing was not possible. Nonetheless, these data provide robust evidence for treatment with abrocitinib leading to the attainment of higher threshold efficacy responses, and that these outcomes are associated with clinically meaningful improvements in QoL outcomes when compared with EASI-75 to <EASI-90 outcomes, or PP-NRS4 but not PP-NRS-0/1 outcomes. Consideration of treatment benefit should account for the proportions of patients who achieve higher threshold efficacy responses, and associated improvements in QoL. In addition, the CDLQI, originally developed and validated for use in patients aged <16 years was used in patients aged <18 years in this study with the agreement of the instrument's developer. This allowed for alignment with other patient-reported outcome (PRO) measures included in abrocitinib trials, thereby creating an adolescent PRO measure set and an adult PRO measure set. The use of CDLQI in patients aged up to 17 years has since been shown to correlate closely with DLQI.[35] Future research directions could include characterization of factors that may be correlated with the likelihood

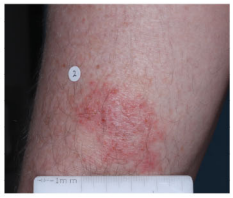
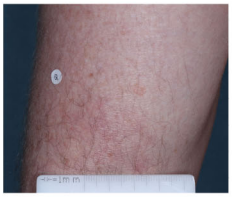
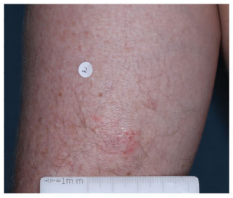
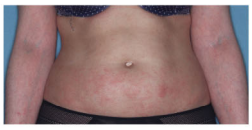
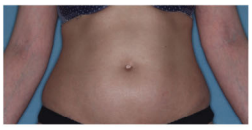
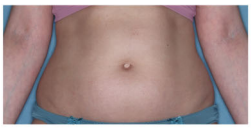
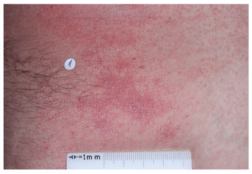
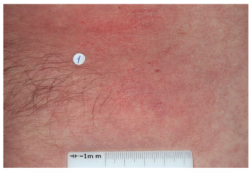
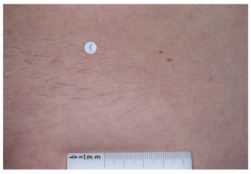
	Baseline	Week 2	Week 12
Participant 1 (100 mg) Photographs showing partial upper limb			
EASI score	19.8	11.2	3.8
EASI score depth of response category at Week 12	EASI-75 to <EASI-90		
Participant 2 (100 mg) Photographs showing partial trunk			
EASI score (total)	36.9	10.2	0.6
EASI depth of response category of the total body at week 12	EASI-90 to <EASI-100		
Participant 3 (200 mg) Photographs showing partial trunk			
EASI score	17.2	11	2.7
EASI score depth of response category at Week 12	EASI-75 to <EASI-90		

Figure 5 Photographs of patients who received abrocitinib 100 mg at baseline, week 2 and week 12. EASI, Eczema Area and Severity Index.

of attaining these higher threshold responses with a view towards determining subsets of patients who have the highest likelihood of obtaining these higher threshold efficacy responses following abrocitinib treatment.

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Data availability statement

Upon request, and subject to review, Pfizer will provide the data that support the findings of this study. Subject to certain criteria, conditions and exceptions, Pfizer may also provide access to the related individual de-identified participant data. See https://www.pfizer.com/science/clinical-trials/trial-data-and-results for more information.

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