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# Characterization of acne associated with upadacitinib treatment in patients with moderate-to-severe atopic dermatitis: A post hoc integrated analysis of 3 phase 3 randomized, double-blind, placebo-controlled trials



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**Background:** Acne is the most frequent adverse event associated with upadacitinib treatment in patients with moderate-to-severe atopic dermatitis.

**Objective:** To characterize the adverse event of acne associated with upadacitinib.

**Methods:** This was a post hoc integrated analysis of 3 phase 3 randomized, double-blind, placebo-controlled trials of upadacitinib, alone (NCT03569293 and NCT03607422) or in combination with topical corticosteroids (NCT03568318). Data included were from the 16-week placebo-controlled period.

**Results:** Over 16 weeks, 84 of 857 (9.8%), 131 of 864 (15.2%), and 19 of 862 (2.2%) patients randomized to receive upadacitinib 15 mg, upadacitinib 30 mg, and placebo, respectively, experienced acne. All cases of acne, except 1, were mild/moderate in severity; 2 patients discontinued treatment due to moderate acne. Acne occurred at higher rates among younger, female, and non-White patients. Acne required no intervention in 40.5% and 46.6% of patients receiving upadacitinib 15 and 30 mg, respectively; most remaining cases were managed with topical antibiotics, benzoyl peroxide, and/or retinoids. Acne also had no impact on patient-reported outcomes.

**Limitations:** This study was relatively short in duration and had a small patient population.

**Conclusions:** Acne associated with upadacitinib for atopic dermatitis treatment is usually mild/moderate in severity and managed with topical therapies or no intervention. (J Am Acad Dermatol 2022;87:784-91.)

**Key words:** acne; adverse event; atopic dermatitis; topical corticosteroids; upadacitinib.

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## INTRODUCTION

Upadacitinib, an orally administered Janus kinase (JAK) inhibitor with greater inhibitory potency for JAK1 versus JAK2, JAK3, and tyrosine kinase 2,<sup>1</sup> is approved in over 50 countries for the treatment of moderate-to-severe atopic dermatitis (AD),<sup>2,3</sup> rheumatoid arthritis,<sup>4-8</sup> psoriatic arthritis,<sup>9</sup> ankylosing spondylitis,<sup>10</sup> and ulcerative colitis<sup>11,12</sup> in adults. The efficacy and safety of upadacitinib in patients with moderate-to-severe AD were investigated in a phase 2b trial in adults<sup>13</sup> and 3 phase 3 international, multicenter, randomized, double-blind, placebo-controlled trials in adolescents (aged 12-17 years) and adults (aged 18-75 years). The Measure Up 1 and Measure Up 2 studies investigated upadacitinib monotherapy,<sup>2</sup> while the AD Up study investigated upadacitinib in combination with topical corticosteroids.<sup>3</sup>

One of the most common adverse events (AEs) reported in the upadacitinib phase 3 trials for the treatment of moderate-to-severe AD was an acne-like eruption of unknown etiology.<sup>2,3,13</sup> The incidence of acne during the 16-week double-blind placebo-controlled period ranged from 7% to 13% with upadacitinib 15 mg and from 14% to 17% with upadacitinib 30 mg, compared with 2% with placebo.<sup>2,3</sup> Of note, acne occurred at lower rates in studies of upadacitinib for other indications; the rate of acne events in rheumatology indications (rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis) was <2% and in a gastroenterology indication (ulcerative colitis) was ≤6%.<sup>14,15</sup>

This post hoc integrated analysis characterizes the occurrence, time course, clinical features, and management of acne associated with upadacitinib treatment using data from the 3 phase 3 trials in adolescent and adult patients with moderate-to-severe AD.

## METHODS

Details of the Measure Up 1 (NCT03569293), Measure Up 2 (NCT03607422), and AD Up (NCT03568318) study designs were described previously.<sup>2,3</sup> Independent ethics committees or institutional review boards approved the study protocols, informed consent forms, and recruitment materials before patient enrollment. All 3 trials were conducted in accordance with the International Conference

for Harmonisation guidelines, applicable regulations, and the Declaration of Helsinki. Adult patients and parents or legal guardians of adolescent patients provided written informed consent before screening.

Briefly, eligible patients were randomized (1:1:1) to receive once daily oral upadacitinib 15 mg, upadacitinib 30 mg, or placebo as monotherapy (Measure Up 1 and Measure Up 2) or with concomitant topical corticosteroids (AD Up). Eligible patients included adolescents (aged 12-17 years, body weight ≥40 kg) or adults (aged 18-75 years) with diagnosed moderate-to-severe AD who were candidates for systemic therapy (eg, patients with a history of inadequate response to topical treatments for AD, patients who were using systemic treatment for AD, or patients for whom topical treatments were otherwise medically inadvisable for their AD).

Acne was neither anticipated nor prespecified as an AE of special interest; therefore, for this post hoc analysis, a supplemental case report form was used to collect data on acne-related events as identified by the investigators, based on data collected during the 16-week placebo-controlled period. AEs were assessed using the National Cancer Institute Common Terminology Criteria for Adverse Events, version 5.0. According to these guidelines, the severity of acne was defined as grade 1 (papules and/or pustules covering 10% body surface area [BSA], which may or may not be associated with symptoms of pruritus or tenderness), grade 2 (papules and/or pustules covering 10%-30% BSA, which may or may not be associated with symptoms of pruritus or tenderness, but having psychosocial impact and limiting instrumental activities of daily living or papules, and/or pustules covering >30% BSA with or without mild symptoms), or grade 3 (papules and/or pustules covering >30% BSA with moderate-to-severe symptoms that limit self-care activities of daily living and are associated with local superinfection with oral antibiotics indicated). The incidence of acne was reported as frequencies (*n*, %), and the time of onset, duration, severity, location/distribution, morphology, recurrence, and any therapies used to manage treatment-emergent acne were recorded. Data relating to the occurrence of acne were presented using descriptive statistics.

## CAPSULE SUMMARY

- In this post hoc integrated analysis of 3 phase 3 trials, we characterize the incidence and clinical features of treatment-emergent acne in patients with moderate-to-severe atopic dermatitis receiving upadacitinib.
- The reported results may aid the management of upadacitinib-associated acne in both the clinical trial and real-world settings.

*Abbreviations used:*

AD:	atopic dermatitis
AE:	adverse events
BSA:	body surface area
DLQI:	Dermatology Life Quality Index
EASI:	Eczema Area and Severity Index
JAK:	Janus kinase
PGIT:	Patient Global Impression of Treatment
QoL:	quality of life
SD:	standard deviation

A number of patient-reported outcomes were collected. Dermatology Life Quality Index (DLQI) scores were recorded at baseline and week 16 in patients who were aged 16 years or older at screening. In addition, the Patient Global Impression of Treatment (PGIT) was administered using a 7-point scale from 1 = “extremely dissatisfied” to 7 = “extremely satisfied.”

## RESULTS

A total of 2583 patients with moderate-to-severe AD were randomized and received at least 1 dose of the study drug. The mean age was 34.2 years (range: 12-75 years, standard deviation [SD]: 15.5 years); 13.3% of patients were younger than 18 years of age. Overall, acne occurred in 84 patients (9.8%) randomized to upadacitinib 15 mg, 131 patients (15.2%) randomized to upadacitinib 30 mg, and 19 patients (2.2%) randomized to placebo. Almost all cases of acne were mild/moderate in severity (grade 1-2), with only 1 case of severe acne (grade 3) reported. Overall, 2 patients discontinued treatment (1 taking upadacitinib 15 mg and 1 taking upadacitinib 30 mg) due to moderate AEs of acne.

Acne occurred more frequently in females and non-White patients treated with upadacitinib; higher rates were observed in the 30-mg group versus the 15-mg group (Table I). Patients aged 15-40 years receiving upadacitinib 30 mg and those aged 15-17 years receiving upadacitinib 15 mg had the highest frequency of acne. Acne was less common in patients aged 12-14 years and adults aged 65 years or older. Four patients aged 12-14 years (2 in each dose group) and 3 patients aged 65 years or older (all in the upadacitinib 30 mg group) experienced acne as an AE. The most common risk factors for development of acne were a medical or family history of acne (Table II).

The clinical course of acne, including time to onset, duration, and frequency of recurrence, is summarized in Table III. The mean (SD) time to the onset of the first report of acne as an AE was 43.5 (29.9), 40.3 (27.8), and 56.5 (37.3) days in the upadacitinib 15 mg, upadacitinib 30 mg, and placebo

groups, respectively (Supplementary Fig 1, available via Mendeley at <https://data.mendeley.com/datasets/fm8pfvjm69/1>). The mean (SD) duration of acne was 104.2 (100.9) days and 93.2 (88.2) days in the upadacitinib 15 mg and 30 mg dose groups, respectively, versus 23.7 (13.7) days in the placebo group. Recurrence of acne within the 16-week placebo-controlled period was uncommon, occurring in <1% of upadacitinib-treated patients. Almost all patients (>95%) had acne on the face, with approximately 30% having acne on the trunk, and only a few having acne on the extremities (Table III). The most common acne morphology was inflammatory papules, comedones, and pustules. Inflammatory nodules and cysts, as well as scarring, occurred in <10% of patients who developed acne.

None of the AEs of acne was serious. Most cases of acne were mild or moderate and clinically manageable, with or without specific treatment. Of note, 40.5% and 46.6% of cases in the upadacitinib 15 mg and 30 mg groups, respectively, did not require management with concomitant medication. Of those who required intervention for acne, most patients received topical therapies (alone or in combination), including antibiotics, benzoyl peroxide, or retinoids (Table IV). Few patients who developed acne required systemic therapies: 4 patients (4.8%) in the upadacitinib 15 mg group and 10 patients (7.6%) in the upadacitinib 30 mg group received oral treatments. The most common oral treatments were tetracycline antibiotics (78.6%). No patients in the placebo group received oral treatments.

To understand the impact of acne on the patients' quality of life (QoL), many patient-reported outcome instruments were used. Overall, patients reported improvements in the impact of AD disease symptoms and treatment on QoL as measured by the DLQI, regardless of whether they experienced acne (Table V). DLQI scores improved progressively in patients achieving Eczema Area and Severity Index (EASI)-75, EASI-90, and EASI-100, respectively; there was no difference in the impact of upadacitinib treatment on QoL between those who did or did not experience acne at any of the EASI thresholds. Similarly, there were no differences in upadacitinib treatment satisfaction as measured using the PGIT among patients with or without acne, regardless of the degree of response.

## DISCUSSION

Across 3 phase 3 trials, acne occurred more frequently in patients with moderate-to-severe AD who were treated with upadacitinib compared with those who received placebo; higher rates of acne

**Table I.** Characteristics of patients with acne as an adverse event (integrated data\*)

<i>n/N (%)</i>	Placebo <i>N = 862</i>	Upadacitinib 15 mg <i>N = 857</i>	Upadacitinib 30 mg <i>N = 864</i>
Any acne AE	19 (2.2)	84 (9.8)	131 (15.2)
Acne as an AE according to sex			
Male	14/476 (2.9)	40/491 (8.1)	68/507 (13.4)
Female	5/386 (1.3)	44/366 (12.0)	63/357 (17.6)
Acne as an AE by age group			
12-14 y	0/36 (0)	2/33 (6.1)	2/31 (6.5)
15-17 y	1/79 (1.3)	13/81 (16.0)	15/83 (18.1)
≥18- <40 y	14/462 (3.0)	53/484 (11.0)	87/473 (18.4)
≥40- <65 y	4/249 (1.6)	16/226 (7.1)	24/226 (10.6)
≥65 y	0/36 (0)	0/33 (0)	3/51 (5.9)
Acne as an AE by race			
White	9/601 (1.5)	47/570 (8.2)	78/607 (12.9)
Non-White	10/261 (3.8)	37/287 (12.9)	53/257 (20.6)

AE, Adverse event.

\*Data from the ongoing Measure Up 1, Measure Up 2, and AD Up studies.

**Table II.** Predisposing factors among patients with acne as an adverse event (integrated data\*)

<i>n (%)</i>	Placebo <i>N = 19</i>	Upadacitinib 15 mg <i>N = 84</i>	Upadacitinib 30 mg <i>N = 131</i>
Medical history of acne	9 (47.4)	29 (34.5)	43 (32.8)
Family history of acne	5 (26.3)	25 (29.8)	33 (25.2)
Concomitant medication associated with acne	1 (5.3)	8 (9.5)	7 (5.3)
Other predisposing factors for acne	3 (15.8)	12 (14.3)	18 (13.7)

\*Data from the ongoing Measure Up 1, Measure Up 2, and AD Up studies.

were observed with 30-mg upadacitinib than with 15 mg. However, the time to onset, duration, and risk of recurrence were similar between the 2 doses of upadacitinib. Acne was mild or moderate in almost all cases, with only 1 case of severe acne reported in the 1721 upadacitinib-treated patients. Overall, no acne event was deemed serious, and treatment discontinuation due to upadacitinib-associated acne was rare (0.1%). Acne typically occurred after approximately 6 weeks of upadacitinib treatment and lasted for approximately 3 months; recurrence of acne within the 16-week placebo-controlled period was rare, occurring in <1% of upadacitinib-treated patients. Importantly, the occurrence of acne had no effect on patient QoL, with similar DLQI scores for upadacitinib responders with/without acne and non-responders with/without acne. In addition, acne also had no impact on patient satisfaction with upadacitinib as measured using the PGIT.

Acne was clinically manageable, and almost half the patients who developed it required no intervention; most patients who required intervention only used topical therapies (most commonly antibiotics, benzoyl peroxide, and retinoids, given alone or in

combination). Systemic therapies were used infrequently, as 4.8% and 7.6% of patients who developed acne while taking upadacitinib 15 mg and 30 mg, respectively, required oral treatment, mainly tetracycline antibiotics; only 1 patient received an oral retinoid.

The prevalence of acne in the general population peaks during adolescence, with 68.5% of males and 66.8% of females in the teenage years having acne, and then decreases with advancing age to 7.3% of males and 15.3% of females aged 50 years or older having acne.<sup>16</sup> Similar to the general population, acne incidence in patients taking upadacitinib decreased with advancing age. Three patients aged 65 years or older, all in the upadacitinib 30-mg group, experienced acne. The highest incidence of acne was seen in adolescents and adults aged younger than 40 years. Although acne was reported in upadacitinib trials for other indications, the incidence was low and did not meet thresholds of the most frequently reported AEs for inclusion in published reports (≥5%). However, patients in the upadacitinib trials for rheumatoid arthritis and psoriatic arthritis were older than 50 years

**Table III.** Characterization of acne as an adverse event (integrated data\*)

<i>n</i> (%)	Placebo N = 862	Upadacitinib 15 mg N = 857	Upadacitinib 30 mg N = 864
Any acne AE	19 (2.2)	84 (9.8)	131 (15.2)
Discontinuation due to acne AE	0	1 (0.1)	1 (0.1)
Mean time to the onset of the first acne event, d (SD)	56.5 (37.3)	43.5 (29.9)	40.3 (27.8)
Mean duration of the first acne event, d (SD)	23.7 (13.7)	104.2 (100.9)	93.2 (88.2)
Recurrence of acne AE	0	4 (0.5)	6 (0.7)
Areas of acne involvement <sup>†</sup>			
Face	17 (89.5)	81 (96.4)	126 (96.2)
Trunk	7 (36.8)	24 (28.6)	40 (30.5)
Extremities	1 (5.3)	7 (8.3)	7 (5.3)
Morphology of acne <sup>†</sup>			
Inflammatory papules	16 (84.2)	77 (91.7)	110 (84.0)
Pustules	7 (36.8)	30 (35.7)	54 (41.2)
Inflammatory nodules and cysts	1 (5.3)	6 (7.1)	11 (8.4)
Comedones	6 (31.6)	35 (41.7)	56 (42.7)
Scarring	3 (15.8)	4 (4.8)	12 (9.2)

AE, Adverse event; SD, standard deviation.

\*Data from the ongoing Measure Up 1, Measure Up 2, and AD Up studies.

<sup>†</sup>Percentages calculated out of the number of patients experiencing acne, not the total population.

**Table IV.** Treatments utilized for management of acne as an adverse event (integrated data\*)

<i>n</i> (%)	Placebo N = 19	Upadacitinib 15 mg N = 84	Upadacitinib 30 mg N = 131
No acne medication	10 (52.6)	34 (40.5)	61 (46.6)
Topical <sup>†</sup>	5 (26.3)	32 (38.1)	50 (38.2)
Anti-infective	2 (10.5)	8 (9.5)	24 (18.3)
Peroxides	1 (5.3)	11 (13.1)	14 (10.7)
Retinoids	1 (5.3)	10 (11.9)	4 (3.1)
Oral <sup>‡</sup>	0	4 (4.8)	10 (7.6)
Tetracycline <sup>§</sup>	0	2 (2.4)	9 (6.9)
Retinoids <sup>  </sup>	0	1 (1.2)	0
Progestogens/estrogens	0	1 (1.2)	0
Phenothiazine derivatives <sup>¶</sup>	0	0	1 (0.8)
Nucleosides and nucleotides <sup>#</sup>	0	0	1 (0.8)
Transdermal <sup>**</sup>	1 (5.3)	0	0
Cutaneous <sup>††</sup>	0	0	3 (2.3)
Missing	3 (15.8)	15 (17.9)	13 (9.9)

\*Data from the ongoing Measure Up 1, Measure Up 2, and AD Up studies.

<sup>†</sup>Topical treatments used by  $\geq 10\%$  of patients in any treatment group.

<sup>‡</sup>All oral treatments are listed, and patients could receive more than 1 oral treatment.

<sup>§</sup>Tetracyclines used include doxycycline, lymecycline, doxymycin, minocycline, and sarecycline.

<sup>||</sup>The patient received isotretinoin.

<sup>¶</sup>The patient received mequitazine.

<sup>#</sup>The patient received famciclovir.

<sup>\*\*</sup>The patient received nadifloxacin.

<sup>††</sup>Patients received fusidic acid and/or benzoyl peroxide creams.

(mean age), while those in the upadacitinib trials for ulcerative colitis were approximately 40 years of age.<sup>4-6,8-12,17</sup> By contrast, the mean age in the upadacitinib trials for AD was 33.9 years, with 80% of acne cases occurring in patients younger than 40 years. It is therefore possible that acne has not been previously identified as a risk associated with upadacitinib because most patients in studies for

other indications were older and hence at a lower risk. The younger population in the AD studies for upadacitinib may partly account for the higher frequency of acne observed. Additionally, as the investigators for this analysis are primarily dermatologists, they may have been more prone to identify acne as an AE than would investigators in other specialties.

**Table V.** Summary of patient-reported outcomes DLQI and PGIT in responders and nonresponders according to EASI-75, EASI-90, and EASI-100 in patients with and without the adverse event of acne\*

Mean (SD)	DLQI <sup>†</sup>		PGIT	
	Measure Up 1 and Measure Up 2 integrated data			
	Acne (n = 223)	No acne (n = 1315)	Acne (n = 240)	No acne (n = 1411)
Baseline	16.9 (6.8)	16.7 (7.0)	3.2 (1.4)	3.3 (1.6)
Week 16	6.3 (6.3)	7.3 (7.2)	5.3 (1.7)	4.9 (1.9)
EASI-75				
Responders	4.3 (5.2)	3.9 (4.7)	5.8 (1.5)	5.4 (1.9)
Nonresponders	11.0 (6.1)	11.9 (7.5)	4.1 (1.5)	4.1 (1.6)
EASI-90				
Responders	3.5 (4.9)	3.0 (4.1)	5.9 (1.6)	5.6 (2.0)
Nonresponders	9.8 (6.1)	10.4 (7.5)	4.6 (1.6)	4.3 (1.7)
EASI-100				
Responders	1.7 (3.1)	1.7 (3.4)	6.0 (1.8)	5.6 (2.1)
Nonresponders	7.3 (6.4)	8.1 (7.3)	5.2 (1.6)	4.7 (1.8)
	AD Up			
	Acne (n = 115)	No acne (n = 710)	Acne (n = 126)	No acne (n = 767)
Baseline	17.5 (6.4)	16.5 (7.2)	3.7 (1.5)	3.4 (1.5)
Week 16	6.1 (5.9)	6.7 (6.6)	5.5 (1.7)	4.9 (1.9)
EASI-75				
Responders	4.6 (4.9)	4.2 (4.7)	5.8 (1.7)	5.3 (1.9)
Nonresponders	11.2 (6.2)	10.5 (7.3)	4.5 (1.5)	4.3 (1.6)
EASI-90				
Responders	3.8 (4.5)	3.3 (4.5)	5.8 (1.7)	5.4 (2.1)
Nonresponders	9.7 (5.9)	9.0 (6.8)	4.9 (1.6)	4.6 (1.7)
EASI-100				
Responders	1.6 (1.9)	1.4 (2.8)	5.4 (2.4)	5.8 (2.1)
Nonresponders	6.9 (6.0)	7.4 (6.6)	5.5 (1.6)	4.8 (1.8)

DLQI, Dermatology Life Quality Index; EASI, eczema area and severity index; PGIT, Patient Global Impression of Treatment; SD, standard deviation.

\*Populations stratified by the baseline presence of acne.

<sup>†</sup>DLQI was administered only in patients 16 years of age or older.

The overall incidence of acne was greater in females than that in males, which is consistent with the general population.<sup>16</sup> Non-White patients were at a numerically higher risk of experiencing acne, also consistent with the general population.<sup>18</sup> The proportion of placebo-treated patients who had a medical or family history of acne was higher or similar to the proportion of upadacitinib-treated patients. Results from a recent study indicated that there is no relationship between acne incidence and AD.<sup>19</sup> Together, these data suggest that patients who are younger, have a history of acne, are female, or are non-White may have an increased risk of acne, regardless of treatment.

The underlying pathogenesis for upadacitinib-associated acne in patients with AD is unclear. Acne has been reported in trials investigating other systemic JAK inhibitors for the treatment of moderate-to-severe AD.<sup>20-22</sup> Acne occurred in 1.3%

to 2.9% and 5.8% to 6.6% of patients taking abrocitinib 100 mg once daily and 200 mg once daily (vs 0% in patients receiving placebo), respectively, suggesting a dose-response relationship similar to that noted with upadacitinib. Furthermore, 4% of patients taking baricitinib 4 mg once daily experienced acne.<sup>20-22</sup> A recent systematic review and meta-analysis reported that 13.2% of patients with alopecia areata developed acne while taking tofacitinib.<sup>23</sup> With respect to topical JAK inhibitors, acne has been reported in 4.3% of patients using delgocitinib for AD<sup>24</sup> and in 10% to 18% of patients using ruxolitinib for vitiligo.<sup>25</sup> JAK1 and JAK3 are upregulated in acne lesions relative to nonlesional skin and healthy volunteers, whereas there is no increase in JAK2 expression.<sup>26</sup> While this indicates a potential link between the JAK pathway and acne, it does not explain the cause of treatment-emergent acne seen with JAK inhibition, both topical and systemic.

Further research is required to elucidate the mechanism underlying the development of acne in upadacitinib-treated patients, especially those with AD.

This post hoc analysis based on data from 3 phase 3 trials is limited because acne was not anticipated or prespecified as an AE of special interest. The study protocols did not include mechanisms to capture whether resolution of acne was spontaneous or due to administration of acne-specific treatments. No biomarker analysis was conducted, and no samples for histologic or microbiome evaluation were collected to clarify the underlying etiology of acne. Overall, the population of upadacitinib-treated patients who experienced an acne-like eruption was relatively small, precluding meaningful multivariate analyses to clearly identify risk factors for treatment-emergent acne, making it difficult to define the at-risk population. Further, our study evaluated the placebo-controlled 16-week period alone, with lack of long-term follow-up data.

In summary, acne is one of the most common AEs seen with upadacitinib treatment in adolescents and adults with moderate-to-severe AD, affecting about 10% of patients in the first blinded 16-week phase 3 trials. In our studies, all cases except 1 were mild or moderate in severity and either did not require treatment or were clinically manageable with topical therapies. Elucidation of the mechanism behind JAK inhibitor-associated acne requires further research.

## DATA SHARING STATEMENT

AbbVie is committed to responsible data sharing regarding the clinical trials we sponsor. This includes access to anonymized individual and clinical trial-level data (analysis data sets), as well as other information (eg, protocols and clinical study reports), as long as the clinical trials are not part of an ongoing or planned regulatory submission. This includes requests for clinical trial data for unlicensed products and indications.

Clinical trial data can be requested by any qualified researchers who engage in rigorous, independent scientific research and will be provided following review and approval of a research proposal and statistical analysis plan and execution of a data sharing agreement. Data requests can be submitted at any time, and the data will be accessible for 12 months, with possible extensions considered. For more information on the process, or to submit a request, visit the following link: <https://www.abbvie.com/our-science/clinical-trials/clinical-trials-data-and-information-sharing/data-and-information-sharing-with-qualified-researchers.html>.

AbbVie Inc participated in the study design; study research; collection, analysis, and interpretation of data; and writing, reviewing, and approving this manuscript in its entirety. All authors had access to the data; participated in the development, review, and approval of the manuscript; and agreed to submit this manuscript for publication. AbbVie and the authors thank all study investigators for their contributions and the patients who participated in these studies. Brian Waterhouse, a former AbbVie employee, managed the overall integrated safety analysis for upadacitinib. AbbVie funded the research for these studies and provided writing support for this manuscript. Medical writing assistance, funded by AbbVie, was provided by Spencer Hughes, PhD, and James C Street, PhD, of JB Ashtin. No honoraria or payments were made for authorship.

## Conflicts of interest

Dr Mendes-Bastos has received honoraria for consulting and/or speaker services from AbbVie, Novartis, Janssen, LEO Pharma, Ammirall, Sanofi, Viartis, L'Oreal, and Cantabria Labs. He has also worked as a principal investigator in clinical trials supported by AbbVie, Sanofi, and Novartis. Dr Guttman-Yassky is employed by Mount Sinai and is a researcher and/or consultant for AbbVie, Anacor Pharmaceuticals, AnaptysBio, Asana Biosciences, Botanix Pharmaceuticals, Celgene, DBV Technologies, Dermira, Dr Reddy's Laboratories (Promius Pharma), DS Biopharma, Escalier Biosciences, Galderma, Glenmark, Innovaderm, Janssen, Kyowa Kirin, LEO Pharma, Lilly, MedImmune, Mitsubishi Tanabe Pharma, Novan, Novartis, Pfizer, Ralexar Therapeutics, Regeneron, Sanofi, Stiefel/GlaxoSmithKline, UCB, and Vitae Pharmaceuticals. Ms Jiang, Dr Ladizinski, Dr Liu, Dr Teixeira, and Dr Vigna are full-time employees of AbbVie and may hold AbbVie stock or stock options. Dr Prajapati has served as an investigator for AbbVie, Amgen, Arcutis, Arena, Asana, Bausch Health, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Concert, Dermavant, Dermira, Eli Lilly, Galderma, Incyte, Janssen, LEO Pharma, Nimbus Lakshmi, Novartis, Pfizer, Regeneron, Sanofi Genzyme, UCB Pharma, and Valeant. He has served as a consultant, advisor, and/or speaker for AbbVie, Actelion, Amgen, Aralez, Arcutis, Aspen, Bausch Health, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Cipher, Eli Lilly, Galderma, GlaxoSmithKline, Homecan, Janssen, LEO Pharma, L'Oreal, Medexus, Novartis, PEDIAPHARM, Pfizer, Sanofi Genzyme, Sun Pharma, Tribute, UCB Pharma, and Valeant. Dr Simpson has received grants, personal fees, and/or nonfinancial support from AbbVie, Amgen, Arena Pharmaceuticals, BenevolentAI Bio, BiomX, Bluefin Biomedicine, Boehringer Ingelheim, Boston Consulting Group, Collective Acumen, Coronado, Dermira, Evidera, ExcerptaMedica, Forte Biosciences, Incyte, Janssen, Kyowa Kirin, LEO Pharma, Lilly, Medscape, Merck, Novartis, Ortho Dermatologics, Pfizer, Regeneron, Sanofi-Genzyme, SPARC India, Tioga Pharmaceuticals, and Vanda Pharmaceuticals. He has also served on advisory boards for AMAZE, FRED, Harmonising



Outcome Measures for Eczema (HOME), Janssen, Kyowa Kirin, LEO Pharma, Lilly, National Eczema Association, NIH MOSS Special Emphasis Panel Study Section, Pfizer, and TARGET PharmaSolutions. Dr Barbarot has received personal fees from AbbVie, Almirall, Janssen, LEO Pharma, Lilly, Pfizer, Sanofi-Genzyme, and UCB; nonfinancial support from Novartis; and grants from LEO Pharma.

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