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ORIGINAL RESEARCH

Crisaborole Ointment Improves Quality of Life of Patients with Mild to Moderate Atopic Dermatitis and Their Families

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ABSTRACT

Introduction: The impact of crisaborole ointment, a nonsteroidal phosphodiesterase 4 inhibitor for the treatment of mild to moderate atopic dermatitis (AD), on quality of life (QoL) was assessed in two identically designed phase 3 studies (AD-301: NCT02118766; AD-302: NCT02118792, both at http://www.clinicaltrials.gov).

Methods: In both studies, patients aged ≥ 2 years with mild to moderate AD per the Investigator's Static Global Assessment were randomly assigned 2:1 to receive crisaborole or vehicle twice daily for 28 days. QoL was assessed using the Children's Dermatology Life Quality Index (CDLQI) (2–15 years), the Dermatology Life Quality Index (DLQI) (≥ 16 years), and the Dermatitis Family Impact Questionnaire (DFI) (parents/caregivers/family of patients aged

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2–17 years). Established QoL score severity bands provided clinical context.
Results: Greater mean improvement in QoL was observed in crisaborole-treated patients than in vehicle-treated patients at day 29 [mean change from baseline (ΔBL), CDLQI: − 4.6 vs. − 3.0; $P < 0.001$; DLQI: − 5.2 vs. − 3.5; $P = 0.015$]. At baseline, more than half the patients had a "moderate effect" or higher of AD on QoL. At day 29, there was a trend toward more crisaborole- than vehicle-treated patients having "small effect" to "no effect", The QoL of parents/caregivers/family improved more for crisaborole-treated than for vehicle-treated patients (ΔBL, DFI: − 3.7 vs. − 2.7; $P = 0.003$).
Conclusion: Crisaborole treatment results in clinically meaningful improvement in QoL for patients and their parents/caregivers/families.
Trial Registration: AD-301: http://www.clinicaltrials.gov, NCT02118766; AD-302: http://www.clinicaltrials.gov, NCT02118792.
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Keywords: Atopic dermatitis; Crisaborole; Eczema; PDE4; Phosphodiesterase 4; Quality of life; Topical treatment

INTRODUCTION

Atopic dermatitis (AD), a chronic inflammatory skin disorder [1–3], affects an estimated 15–30% of children and 2–10% of adults worldwide [1, 4]. The clinical symptoms and visible skin lesions of AD are often associated with psychologic and psychosocial comorbidities and negatively impact the quality of life (QoL) of patients and their families [2, 4–7]. In addition, the hallmark symptom of AD—pruritus—contributes to sleep dysfunction and reduced QoL [2, 8].

Treatment of AD with topical calcineurin inhibitors (TCIs) or topical corticosteroids (TCSs), recommended by the current treatment guidelines [9, 10], reduces disease severity and is associated with improved QoL for patients and their caregivers [11–13]. However, the potential impact of TCS treatment on patient QoL is often not realized because of well-documented "steroid phobia" in the majority of caregivers, leading to underdosing, decreased patient and caregiver adherence, and reduced QoL [14].

Crisaborole ointment is a nonsteroidal phosphodiesterase 4 (PDE4) inhibitor for the treatment of mild to moderate AD [15–20]. Previously published results from two large, vehicle-controlled, identically designed, phase 3 clinical studies in patients ≥ 2 years of age with mild to moderate AD showed that significantly more crisaborole-treated patients achieved global disease severity assessments of "clear" or "almost clear", improvement in all assessed symptoms of AD, and lessening of pruritus severity by the end of treatment [20]. These improvements in global disease severity, symptoms of AD, and severity of pruritus can improve the QoL of patients and their families [6]. To better understand how these improvements in clinical endpoints in the two phase 3 clinical studies translate to improvements in the QoL of patients and their families, the impact of crisaborole ointment on QoL of patients ≥ 2 years old and the parents/caregivers/families of patients 2–17 years old in these two studies was assessed.

METHODS

Study Design and Treatment

Two multicenter, randomized, double-blind, vehicle-controlled, phase 3 studies (http://www.clinicaltrials.gov; AD-301: NCT02118766; AD-302: NCT02118792) were conducted to assess the efficacy and safety of crisaborole in patients ≥ 2 years old with mild to moderate AD; the efficacy and safety results from these studies have been published [20]. Patients were randomly assigned 2:1 to receive crisaborole ointment, 2% (Pfizer Inc., New York, NY), or vehicle, applied twice daily for 28 days (Fig. 1). Both studies were developed and conducted in accordance with the principles of Good Clinical Practice and relevant country-specific regulatory requirements, and the protocols were approved by an institutional review board at each site. All procedures followed were in

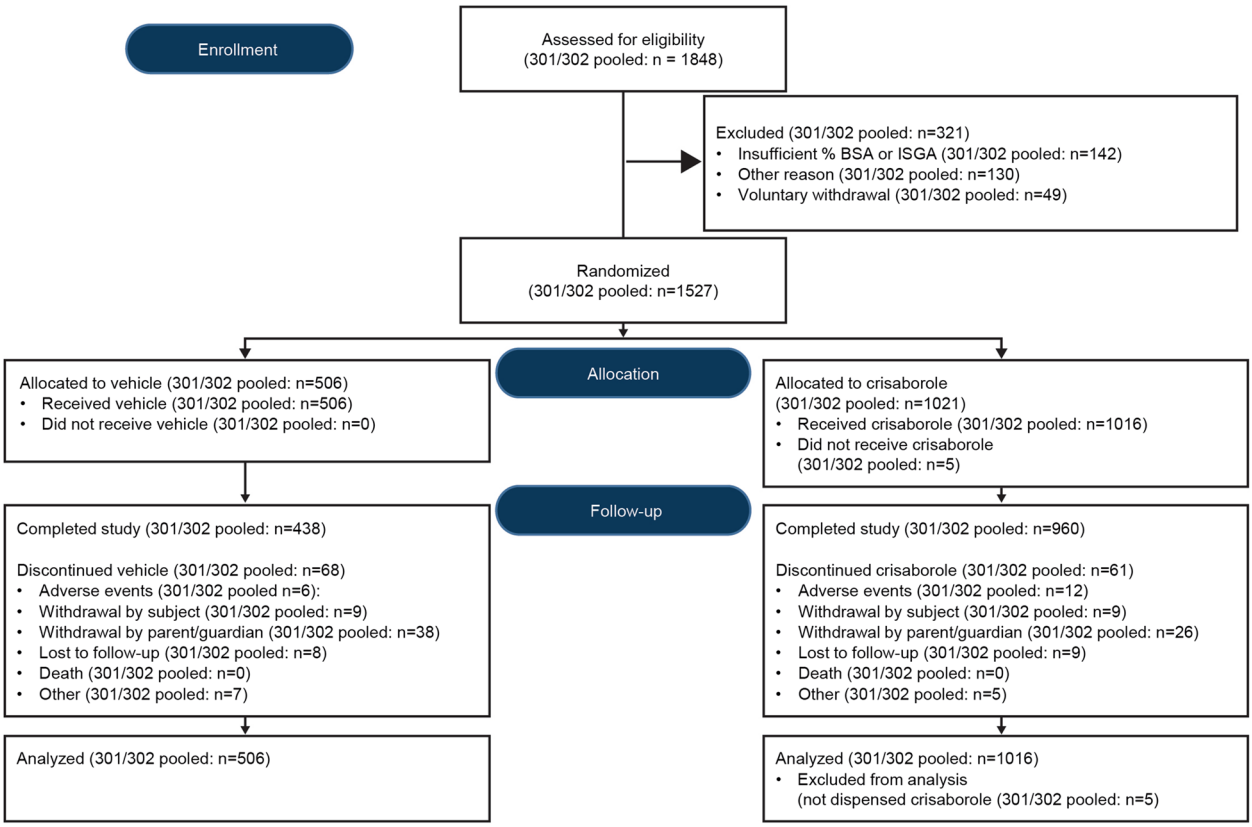

Fig. 1 CONSORT flow diagram. Enrollment, randomization, treatment, and follow-up

accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1964, as revised in 2013. Informed consent was obtained from all patients for being included in the study.

Patients

At baseline/day 1, patients had to be ≥ 2 years old with a clinical diagnosis of AD per the Hanifin and Rajka criteria [21], have ≥ 5% treatable body surface area (BSA) involvement, and have an Investigator's Static Global Assessment (ISGA) score of mild (2) or moderate (3), assessed on a 5-point scale from clear (0) to severe (4). Key exclusion criteria were unstable AD, the consistent need for TCSs, history of anaphylaxis or angioedema, history of biologic therapy, history of recent use of systemic or topical therapies, involvement in another drug or device research study in the preceding 30 days, or known sensitivity to any crisaborole component. The enrolled patient population reflected the overall population with AD, with at least 20% of patients between the ages of 2 and 6 years and no more than 15% adults.

QoL Assessments

Validated QoL scales for inflammatory skin diseases were used for assessments at baseline/day 1 and day 29 and were based on patient age at baseline/day 1 (Fig. 2). Patients 2–15 years of age were assessed using the Children's Dermatology Life Quality Index (CDLQI) [22], and patients aged ≥ 16 years were assessed using the Dermatology Life Quality Index (DLQI) [23]. Because the CDLQI is only validated for use in patients as young as 4 years old [22], change in CDLQI score was also assessed in the group of patients aged 4–15 years. The validated

A

Category	Assessment	CDLQI Patients Aged 2-15 years	DLQI Patients Aged ≥16 years
Symptoms & Feelings	Severity of symptoms (itch, soreness, pain, stinging)	0-3 pts	0-3 pts
	Embarassment or self-conciousness	0-3 pts	0-3 pts
Personal Relationships	Effect on friendships and social interactions (eg, teasing, bulling, avoidance)	0-6 pts	N/A
	Effects on friendships, relatives, and/or partner, and sex life	N/A	0-6 pts
School/Work & Holidays	Effect of skin on work/school or vacation time	0-3 pts	0-3 pts
Leisure	Effect on playing sports and leisure activities	0-6 pts	0-6 pts
	Wearing different clothes/shoes	0-3 pts	N/A
Burden of Treatment	Treatment burden on daily life	0-3 pts	0-3 pts
Sleep	Effect of skin on sleep	0-3 pts	N/A
Daily Activities	Influence on clothes worn and daily tasks	N/A	0-6 pts
Total	Comprehensive assessment of patient QoL	0-30 pts[a]	0-30 pts[a]

B

DFI[a] Family/Parents/Caregivers of Patients Aged 2-17 Years	
Questions (0-3 points each)	**Assessment**
Housework	Effect on housework (eg, washing, cleaning)
Food Preparation	Impact on food preparation and feeding
Sleep	Sleep impact on other family members
Family Leisure	Effect on family leisure activities
Shopping	Effect on time spent shopping for the family
Expenditure	Increased expenditures (eg, treatment costs, clothes)
Tiredness	Exhaustion and tiredness of parents/caregivers
Emotional Distress	Effect on patient/caregiver emotional state (eg, depression, frustration, guilt)
Relationships	Relationship between caregivers/partners and relationships with other children
Burden of Treatment	Burden of child's treatment on caregiver's life
Total (0-30 points)	Comprehensive assessment of patient QoL

Fig. 2 Validated QoL assessment scales and subscales. Superscript letter a indicates that subscale analysis for DFI has not been validated

Dermatitis Family Impact (DFI) scale was used to assess the effect of AD on the QoL of parents/caregivers/families of patients 2–17 years of age [24]. The CDLQI was originally validated for children aged 4 years and older; therefore, children younger than 4 years were aided by parental report. Each scale was descriptively summarized by treatment group, and change from baseline/day 1 results were reported.

Minimal Clinically Important Difference

The minimal clinically important difference (MCID) is considered the smallest amount of change in the assessment instrument score that patients perceive as beneficial and that would result in a change in patient treatment in the absence of troublesome side effects and excessive cost [25]. The MCID for the CDLQI used in this analysis was a ≥ 2.5-point change from baseline [26]. For the DLQI, a longitudinal study in patients with inflammatory skin diseases demonstrated an MCID of ≥ 3.3-point change from baseline [27]. Additional studies are necessary to validate the observed MCID for the CDLQI and DLQI in patients with AD. The MCID for the DFI questionnaire has not been established [24].

CDLQI and DLQI Severity Bands

Severity bands provide clinical interpretation of individual CDLQI and DLQI scores [28]. The effect on the child's life associated with CDLQI scores was defined as 0–1 = "no effect," 2–6 = "small effect," 7–12 = "moderate effect," 13–18 = "very large effect," and 19–30 = "extremely large effect" [28]. Severity bands for patients ≥ 16 years of age for DLQI scores were defined as 0–1 = "no effect," 2–5 = "small effect," 6–10 = "moderate effect," 11–20 = "very large effect," and 21–30 = "extremely large effect" [29].

Statistics

Analysis of QoL measurements was performed using descriptive statistics. Differences between treatment groups in absolute change from baseline were analyzed by Wilcoxon rank sum test, a nonparametric test. Differences between treatment groups regarding the percentage of patients who experienced MCID for the CDLQI and DLQI at day 29 were analyzed using the Fisher exact test. A Wilcoxon rank sum test was used to analyze differences between treatment groups in severity bands.

RESULTS

Patient Disposition and Characteristics

Studies AD-301 and AD-302 enrolled 1016 patients treated with crisaborole and 506 patients treated with vehicle, with the first patient enrolling in March 2014 and the last visit occurring in April 2015. No significant differences were observed in baseline demographics and disease characteristics across treatment groups (Table 1). The enrolled patient population reflected the overall AD population, with 85% of patients experiencing symptoms before 5 years of age [3]. Most of the enrolled patient population was 2–15 years old (crisaborole: 80.2%; vehicle: 81.4%), and approximately one-fifth of the enrolled population was ≥ 16 years of age (crisaborole: 19.8%; vehicle: 18.6%). The severity of pruritus and QoL assessment were similar across treatment groups at baseline.

Overall QoL Assessment and MCID at Day 29

Overall, children in both the vehicle and the crisaborole groups experienced improvement in QoL during the study. Children and adolescents aged 2–15 years in the crisaborole ointment group showed greater mean reduction in QoL assessment at day 29 than patients given vehicle, as assessed by CDLQI (mean change from baseline, crisaborole: − 4.6; vehicle: − 3.0; $P < 0.001$) (Fig. 3a). Among the subgroup of patients aged 4–15 years, results were numerically similar and retained statistical significance (mean change from baseline, crisaborole: − 4.5; vehicle: − 2.6; $P < 0.001$) (Fig. 3b). More crisaborole-treated patients (61.7%) achieved MCID, defined as a ≥ 2.5-point change from baseline for CDLQI [26], than vehicle-treated patients (52.1%) ($P = 0.003$).

Patients ≥ 16 years of age treated with crisaborole ointment showed greater mean reduction in DLQI scores at day 29 than patients given vehicle (mean change from baseline, crisaborole: − 5.2; vehicle: − 3.5; $P = 0.015$) (Fig. 3c). MCID, defined as a ≥ 3.3-point change

Table 1 Baseline patient characteristics and disease characteristics by age group in crisaborole phase 3 studies (ITT population)

Patient demographics and characteristics	Ages 2–15 years		Ages ≥ 16 years	
	Vehicle (*n* = 412)	Crisaborole ointment (*n* = 815)	Vehicle (*n* = 94)	Crisaborole ointment (*n* = 201)
Sex, %				
Male	47.6	46.9	30.9	33.8
Female	52.4	53.1	69.1	66.2
Ethnicity, %				
Hispanic or Latino	21.4	20.9	13.8	14.9
Not Hispanic or Latino	78.6	79.1	86.2	85.1
Race, %				
American Indian or Alaskan Native	0.7	1.0	2.1	1.5
Asian	4.4	4.8	9.6	6.5
Black or African American	26.2	27.4	33.0	30.8
Hawaiian or other Pacific Islander	1.7	0.7	1.1	0.5
White	61.9	61.7	54.3	56.7
Other	5.1	4.4	0.0	4.0
Severity of pruritus scale, *n* (%)				
0—none	14 (3.9)	31 (4.3)	5 (6.0)	4 (2.3)
1—mild	102 (28.5)	185 (25.4)	17 (20.5)	44 (25.0)
2—moderate	137 (38.3)	253 (34.8)	30 (36.1)	78 (44.3)
3—severe	105 (29.3)	258 (35.5)	31 (37.3)	50 (28.4)
CDLQI				
n	403	797	–	–
Mean (SD)	9.0 (6.02)	9.3 (5.99)	–	–
DLQI				
n	–	–	92	192
Mean (SD)	–	–	9.3 (6.55)	9.7 (6.29)
DFI (parents/caregivers/families of patients ages 2–17 years)				
n	431	862	–	–
Mean (SD)	7.8 (6.17)	8.1 (6.61)	–	–

CDLQI Children's Dermatology Life Quality Index, *DLQI* Dermatology Life Quality Index, *DFI* Dermatitis Family Impact Questionnaire, *ITT* intent-to-treat, *SD* standard deviation

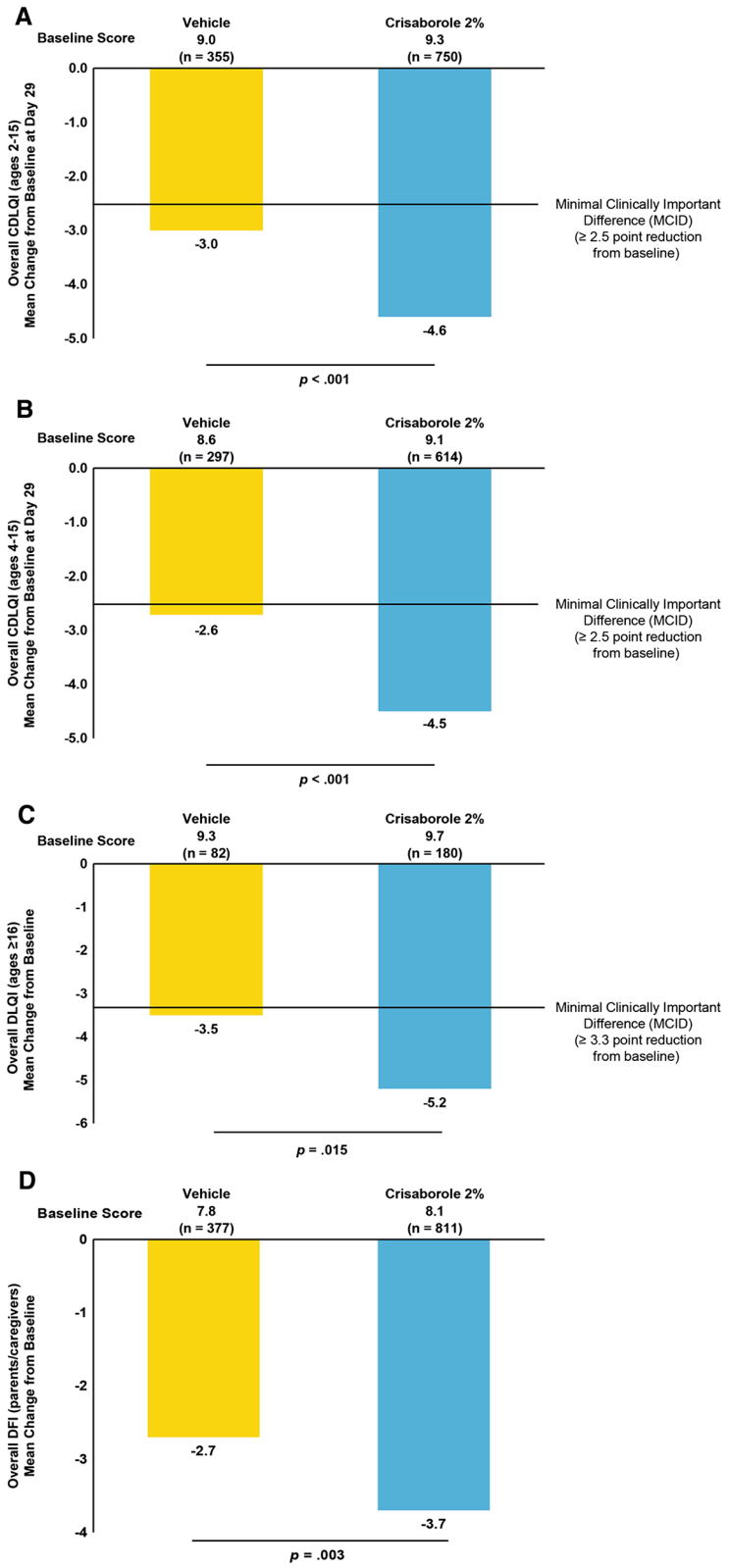

Fig. 3 Mean change from baseline in **a** CDLQI ages 2–15 years, **b** CDLQI ages 4–15 years, **c** DLQI, and **d** DFI scores (pooled analysis, ITT population)

from baseline [27], was achieved by 53.9% of crisaborole-treated patients and 41.5% of vehicle-treated patients ($P = 0.083$). Assessment of improvement in QoL for the parents, caregivers, and families of children and adolescents with AD showed that crisaborole-treated patients showed greater mean reduction overall (mean change from baseline, crisaborole: − 3.7; vehicle: − 2.7; $P = 0.003$) (Fig. 3d).

Severity Bands for CDLQI and DLQI

To provide clinical context to CDLQI and DLQI scores, established severity bands ranging from "no effect" to an "extremely large effect" were analyzed. Most children and adolescents experienced a "moderate effect" of AD on QoL at baseline (crisaborole: 35.3%; vehicle: 34.0%) or worse (crisaborole: 27.2%; vehicle: 24.6%; $P = 0.1769$) (Fig. 4a). By day 29, crisaborole

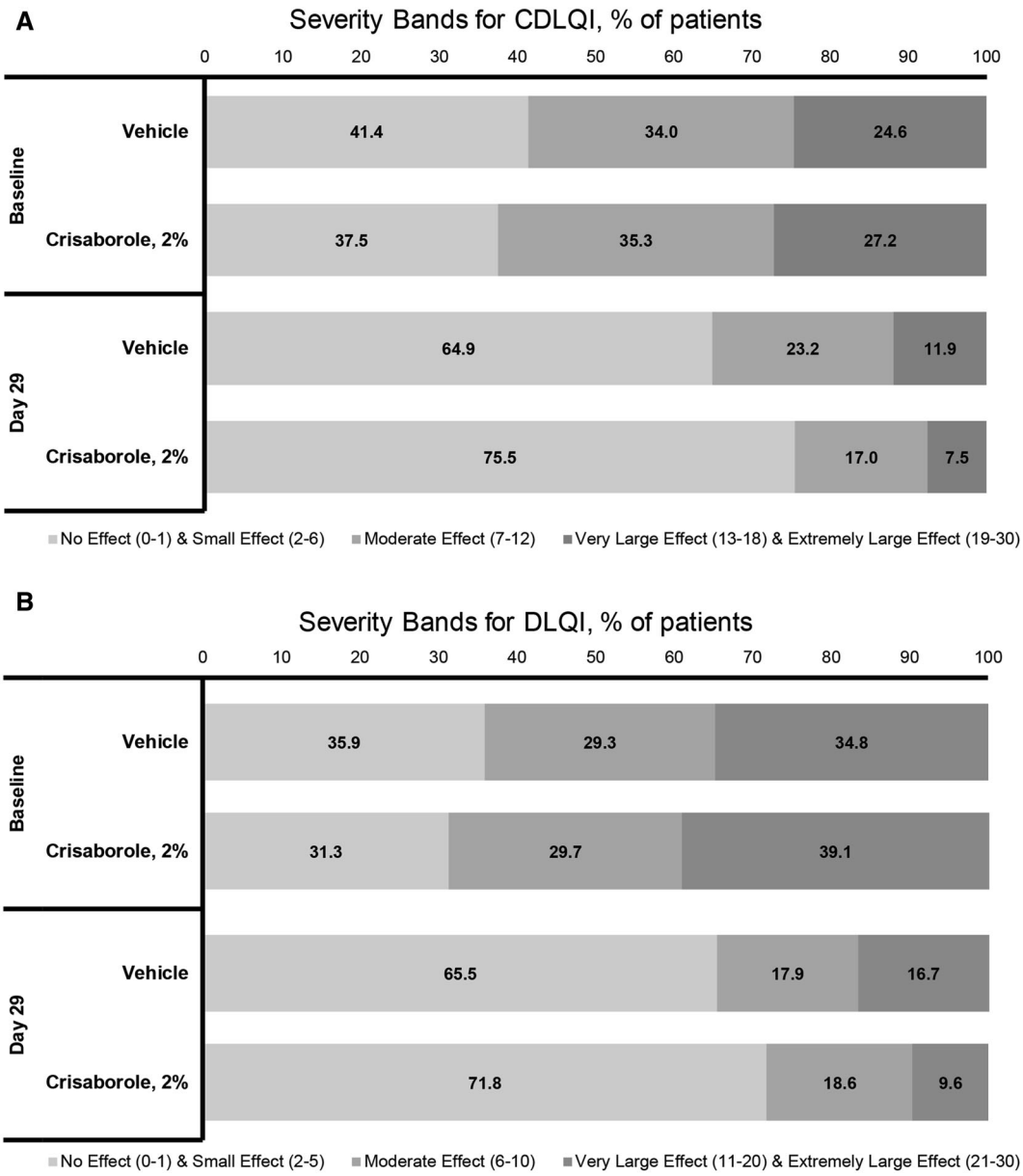

Fig. 4 Severity bands for **a** CDLQI and **b** DLQI overall (pooled analysis, ITT population)

Table 2 Responses per question for CDLQI (ITT population)

Question	Treatment	Patients per response, %				*P* value[a,b]
		Not at all	Only a little	Quite a lot	Very much	
Itching/scratching, painful/sore	*Vehicle*	*13.5*	*48.9*	*24.9*	*12.7*	*< 0.001*
	Crisaborole ointment	*18.6*	*57.9*	*17.1*	*6.4*	
Embarrassed/self-conscious	*Vehicle*	*61.0*	*23.8*	*10.5*	*4.7*	*0.011*
	Crisaborole ointment	*68.2*	*21.2*	*7.7*	*2.9*	
Affected friendships	Vehicle	90.1	6.1	2.2	1.7	0.241
	Crisaborole ointment	92.0	6.6	0.8	0.7	
Affected clothing	Vehicle	61.3	24.6	8.8	5.2	0.210
	Crisaborole ointment	64.2	25.6	6.7	3.6	
Playing	*Vehicle*	*62.4*	*26.8*	*6.6*	*4.1*	*0.010*
	Crisaborole ointment	*69.5*	*23.8*	*4.5*	*2.2*	
Sports	Vehicle	74.0	16.0	5.2	4.7	0.205
	Crisaborole ointment	77.6	13.9	3.8	4.7	
School time	Vehicle	75.0	15.9	6.9	2.2	0.155
	Crisaborole ointment	79.1	16.1	3.1	1.7	
Holiday time	*Vehicle*	*61.2*	*25.9*	*5.8*	*7.2*	*0.039*
	Crisaborole ointment	*69.9*	*22.7*	*6.0*	*1.3*	
Teasing/bullying	Vehicle	82.8	11.9	3.6	1.7	0.210
	Crisaborole ointment	85.5	11.2	1.8	1.4	
Child sleep	*Vehicle*	*42.3*	*34.5*	*13.5*	*9.7*	*0.001*
	Crisaborole ointment	*51.4*	*33.0*	*9.3*	*6.2*	
Burden of treatment	*Vehicle*	*49.7*	*34.5*	*11.0*	*4.7*	*0.001*
	Crisaborole ointment	*60.2*	*29.2*	*7.4*	*3.3*	

CDLQI Children's Dermatology Life Quality Index, *ITT* intent-to-treat

[a] *P* value from a Wilcoxon rank sum test with factor of treatment group

[b] Italic rows indicate statistically significant difference in question response between crisaborole and vehicle treatment groups

treatment led to an improvement in QoL, with 75.5% of patients reporting that their AD had "small effect" to "no effect," compared with 64.9% of vehicle-treated patients ($P = 0.0002$). For patients ≥ 16 years of age, most reported that AD had a "moderate effect" on QoL at baseline (crisaborole: 29.7%; vehicle: 29.3%) or worse (crisaborole: 39.1%; vehicle: 34.8%; $P = 0.4030$) (Fig. 4b). By day 29, a numerically greater proportion of crisaborole-treated patients reported that AD had "small effect" to "no effect" (71.8%) than vehicle-treated patients (65.5%; $P = 0.1400$). These data indicate an overall reduction in the impact of AD on the lives of patients, especially for those who received crisaborole ointment.

CDLQI, DLQI, and DFI: Question Level Analysis

Compared with vehicle-treated patients, more children and adolescents treated with crisaborole ointment experienced less impact on QoL related to itching/scratching and painful/sore ($P < 0.001$), feelings of embarrassment and self-consciousness ($P = 0.011$), playing ($P = 0.010$), holiday time ($P = 0.039$), sleep ($P = 0.001$), and the burden of treatment ($P = 0.001$) (Table 2). Similarly, more crisaborole-treated patients than vehicle-treated patients ≥ 16 years of age reported less impact on QoL for itching/scratching and painful/sore ($P = 0.001$), embarrassment and self-consciousness ($P = 0.024$), and sexual difficulties between partners ($P = 0.017$) (Table 3). The parents/caregivers/families of patients 2–17 years of age treated with crisaborole experienced greater

Table 3 Responses per question for DLQI (ITT population)

Question	Treatment	Patients per response, %				*P* value[a,b]
		Not at all	Only a little	Quite a lot	Very much	
Itching/scratching, painful/sore	*Vehicle*	*8.3*	*65.5*	*16.7*	*9.5*	*0.001*
	Crisaborole ointment	*27.1*	*56.4*	*12.2*	*4.3*	
Embarrassed/self-conscious	*Vehicle*	*47.6*	*25.0*	*11.9*	*15.5*	*0.024*
	Crisaborole ointment	*56.9*	*31.4*	*6.9*	*4.8*	
Shopping, home, yard activities	Vehicle	81.0	13.1	2.4	3.6	0.391
	Crisaborole ointment	75.5	19.7	3.7	1.1	
Influenced clothes worn	Vehicle	47.6	25.0	9.5	17.9	0.063
	Crisaborole ointment	55.9	27.1	11.2	5.9	
Affected social/leisure activity	Vehicle	70.2	17.9	6.0	6.0	0.366
	Crisaborole ointment	73.9	20.7	3.7	1.6	
Affected sports participation	Vehicle	79.8	16.7	0.0	3.6	0.556
	Crisaborole ointment	83.0	12.2	3.7	1.1	
Affected work/studying	Vehicle	70.2	23.8	3.6	2.4	0.193
	Crisaborole ointment	78.7	13.8	1.6	5.9	
Affected relationships	Vehicle	75.0	21.4	1.2	2.4	0.263
	Crisaborole ointment	80.9	17.0	1.1	1.1	
Sexual difficulties	*Vehicle*	*86.9*	*10.7*	*0.0*	*2.4*	*0.017*
	Crisaborole ointment	*95.2*	*3.2*	*0.5*	*1.1*	
Burden of treatment	Vehicle	67.9	27.4	2.4	2.4	0.164
	Crisaborole ointment	59.6	31.4	9.0	0.0	

DLQI Dermatology Life Quality Index, *ITT* intent-to-treat

[a] *P* value from a Wilcoxon rank sum test with factor of treatment group

[b] Italic rows indicate statistically significant difference in question response between crisaborole and vehicle treatment groups

Table 4 Responses per question for DFI (ITT population)

Question	Treatment	Patients per response, %				*P* value[a,b]
		Not at all	Only a little	Quite a lot	Very much	
Housework	Vehicle	61.5	29.6	6.0	2.9	0.555
	Crisaborole ointment	63.6	27.4	5.7	3.3	
Food	Vehicle	73.8	18.8	4.7	2.6	0.142
	Crisaborole ointment	77.5	17.2	3.5	1.8	
Sleep	*Vehicle*	*56.8*	*27.6*	*8.4*	*7.1*	*0.015*
	Crisaborole ointment	*64.2*	*22.8*	*8.5*	*4.5*	
Leisure	Vehicle	66.2	23.8	5.8	4.2	0.281
	Crisaborole ointment	68.7	24.2	3.8	3.3	
Time shopping	*Vehicle*	*78.3*	*18.6*	*1.8*	*1.3*	*0.026*
	Crisaborole ointment	*83.7*	*13.7*	*1.6*	*1.1*	
Expenditure	Vehicle	63.4	29.3	5.0	2.4	0.042
	Crisaborole ointment	69.9	23.4	5.0	2.0	
Tiredness	*Vehicle*	*60.2*	*27.7*	*7.3*	*4.7*	*0.019*
	Crisaborole ointment	*67.2*	*22.9*	*6.2*	*3.7*	
Emotional distress	Vehicle	58.6	29.8	8.9	2.6	0.191
	Crisaborole ointment	63.1	25.9	7.3	3.7	
Relationships	Vehicle	76.7	17.8	4.5	1.0	0.117
	Crisaborole ointment	80.8	14.4	3.3	1.6	
Burden of treatment	Vehicle	46.5	36.0	13.4	4.2	0.201
	Crisaborole ointment	49.0	37.8	9.0	4.3	

DFI Dermatitis Family Impact Questionnaire, *ITT* intent-to-treat

[a] *P* value from a Wilcoxon rank sum test with factor of treatment group

[b] Italic rows indicate statistically significant difference in question response between crisaborole and vehicle treatment groups

improvement than those of vehicle-treated patients in the categories of sleep ($P = 0.015$), time shopping ($P = 0.026$), and expenditure ($P = 0.042$) (Table 4).

DISCUSSION

The current study revealed that even mild AD can significantly affect patients and their families [30]; therefore, regardless of severity of AD, treatment can improve QoL for patients and their families. Crisaborole-treated patients showed greater reduction in pruritus severity than vehicle-treated patients [20] and a reduction in the impact of itching and scratching on QoL for children, adolescents, and adults. AD-associated pruritus greatly affects patient and caregiver QoL and results in sleep disruption [2, 8]. Sleep disruption strongly affects the QoL of children and adults [31], and it is linked to the development of the mental health

comorbidities often seen in patients with AD [32]. Although additional studies are necessary to fully assess the impact of crisaborole on sleep quality, crisaborole-treated children and adolescents and their families experienced lessening of the impact of AD on sleep.

The visibility and stigma associated with skin diseases also impacts the QoL of patients [2]. The reduction in feelings of embarrassment and self-consciousness for crisaborole-treated patients most likely results from reduction in global disease severity and diminution of lesions in visible areas [20]. Treatment of AD itself imposes a significant burden on the QoL of patients because treatment regimens are often time consuming and associated with lifestyle changes [2, 11, 33, 34]. Greater disease severity is directly correlated with more time spent on treatment [34]. A greater proportion of crisaborole-treated children and adolescents experienced lessening of the burden of treatment, which might have resulted from reduction in pruritus severity and global disease severity [20]. AD also has a significant impact on the QoL of parents/caregivers/families of patients with AD because parents spend several hours each day dealing with treatment and lose 1–2 h of sleep on average each night [2, 30]. The lessening of the impact of AD on sleep reported by the parents/caregivers/families of crisaborole-treated patients might reduce sleep loss-associated side effects, such as decreased coping skills and poor work functioning [2].

Available treatments, such as TCSs and TCIs, improve QoL for patients and their families. A greater mean reduction in the Parents of Children With Atopic Dermatitis (PQoL-AD) score was observed for pimecrolimus-treated patients 2–17 years of age with mild to moderate AD treated with pimecrolimus for 6 weeks (least-squares mean change, − 3.2) compared with vehicle-treated patients (− 1.63; $P = 0.023$) [12]. The current study showed that, similar to TCS and TCI, crisaborole ointment improves QoL for patients and their caregivers. Direct comparison of TCS and TCI studies with those of crisaborole are not feasible because of the lack of head-to-head trials and differences in study design, assessment tools used, and patient populations in the individual studies. The large "vehicle effect" seen with the pimecrolimus study and in the current study is commonly observed in AD clinical trials. Topical vehicle is not a placebo, and emollients are the foundation of step care in management of AD [35]. Use of emollients reduces the need for topical steroids in children [36], and emollient therapy is a prevention strategy in high-risk neonates [37]. Petrolatum, a common moisturizer and the main component of the base for the crisaborole ointment and the vehicle ointment, has skin barrier repair and immune-modulating properties [38]. Compared with vehicle alone, the addition of crisaborole improves QoL for patients with AD and their parents/caregivers/families.

Potential limitations with these studies include the use of CDLQI and DLQI in AD because, although both measurement tools are validated for inflammatory skin diseases and commonly used in AD trials, these measures are not specific for AD and might not fully capture the impact of the disease [39, 40]. In addition, the CDLQI has been validated in patients 4 years or older only [22]; therefore, younger patients were aided by a parent/caregiver. However, analysis of the subgroup aged 4–15 years showed a change in CDLQI similar to that seen in the cohort aged 2–15 years.

CONCLUSIONS

Despite the limitations of the study, the improvements in QoL described herein demonstrate that the reduction in objective lesion severity observed in previous analysis [16–18, 20] is clinically meaningful for patients and their families. Crisaborole is a promising novel topical AD treatment that improves mild to moderate AD and the lives of affected patients and their families.

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Data Availability. 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 Inc. 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 United States and/or 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.

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