Improvement in the Symptoms of Anxiety and Depression With Long-Term Abrocitinib Treatment in Adults and Adolescents With Moderate-to-Severe Atopic Dermatitis: A Post Hoc Analysis of JADE EXTEND

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INTRODUCTION

- Patients with atopic dermatitis (AD) have an elevated risk of anxiety and depression that increases with disease severity[1-4]
  - Symptoms of AD, including itch and pain, are associated with sleep disturbance which negatively impacts mental health; however, the relationship among signs and symptoms of AD, anxiety, and depression has not been well characterised[4-6]
- The Hospital Anxiety and Depression Scale (HADS) is a patient-reported measure of anxiety and depression with a score ranging from 0 to 21; a score ≥8 indicates the presence of anxiety or depression[7,8]
- Abrocitinib is an oral, once-daily, Janus kinase 1-selective inhibitor approved for the treatment of adults and adolescents with moderate-to-severe AD
- Abrocitinib treatment in patients with moderate-to-severe AD has been associated with reduced anxiety and depression in the short term[9,10]

OBJECTIVE

- To assess the long-term effect of abrocitinib on anxiety and depression in adults and adolescents with moderate-to-severe AD using HADS

METHODS

Study Design and Patients

- This post hoc analysis included data from patients who received abrocitinib (200 mg or 100 mg), as monotherapy or in combination with topical therapy, in the phase 2a trial JADE MOA (NCT03915496) and phase 3 trials JADE MONO-1 (NCT03349060), JADE MONO-2 (NCT03575871), JADE COMPARE (NCT03720470), JADE TEEN (NCT03796676), and JADE DARE (NCT04345367), and subsequently received the same dose of abrocitinib in the ongoing long-term extension trial, JADE EXTEND (NCT03422822; data cutoff date: 5 September 2022)

Assessments

- Efficacy assessments analysed included
  - Proportions of patients with baseline HADS-Anxiety (HADS-A) or HADS-Depression (HADS-D) scores ≥8 who achieved scores <8, or baseline scores ≥11 who achieved scores of <11, with abrocitinib treatment over 96 weeks
  - Changes in HADS-A or HADS-D score severity category over time from baseline through Week 96
    - Severity level categories for anxiety and depression were HADS-A or HADS-D scores 0-7 (normal), 8-10 (mild), 11-14 (moderate), and 15-21 (severe), respectively[8]
  - Least squares mean (LSM) changes from baseline in HADS-A, HADS-D, and Patient Global Assessment (PtGA) scores were evaluated from Week 2 through Week 96 of abrocitinib treatment
- Safety was also evaluated and stratified by baseline HADS-A and HADS-D scores

Statistical Analysis

- Baseline was defined as the baseline visit from the relevant qualifying parent study and Day 1 as the first day receiving abrocitinib either in the parent phase 2a/3 study or in JADE EXTEND
  - Patients who received placebo in the parent study had their first dose of abrocitinib in JADE EXTEND
- JADE EXTEND is an ongoing study and not all patients had reached the Week 96 timepoint at the time of this planned interim analysis
- All data from JADE EXTEND are reported as observed

RESULTS

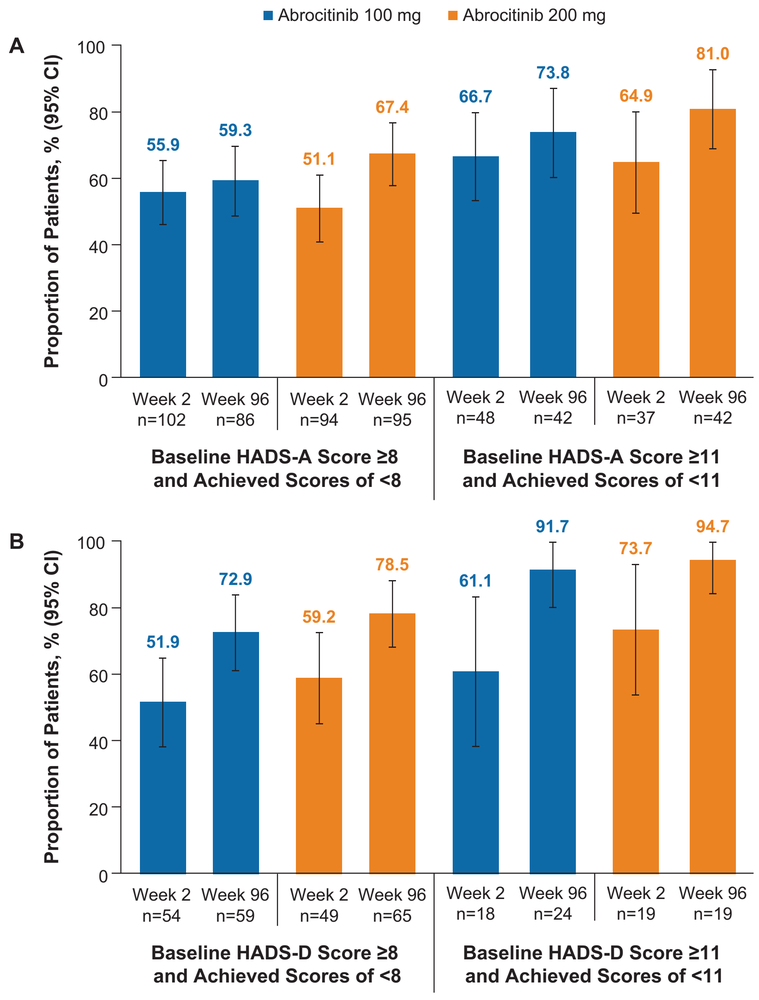
Patients

- Of 1659 patients included in this post hoc analysis, mild to severe symptoms of anxiety at baseline (HADS-A score ≥8) were reported in 264/939 patients (28%) in the abrocitinib 200 mg treatment arm and 201/720 patients (28%) in the abrocitinib 100 mg treatment arm
- Mild to severe symptoms of depression at baseline (HADS-D score ≥8) were reported in 139/939 patients (15%) and 118/720 patients (16%) in the abrocitinib 200 mg and 100 mg treatment arms, respectively

Improvements in Anxiety and Depression

- As early as Week 2, substantial proportions of patients with mild to severe anxiety at baseline (HADS-A ≥8 or ≥11) reported improvements (HADS-A score <8 or <11) with abrocitinib 200 mg and 100 mg; higher proportions reported improvements at Week 96 (**Figure 1A**)
- Similarly, high proportions of patients with mild to severe depression at baseline (HADS-D ≥8 or ≥11) reported improvements with abrocitinib 200 mg and 100 mg at Week 2 and Week 96, respectively (**Figure 1B**)

Figure 1. Proportions of Patients With Improvements in (A) HADS-A Score and (B) HADS-D Score With Abrocitinib Treatment

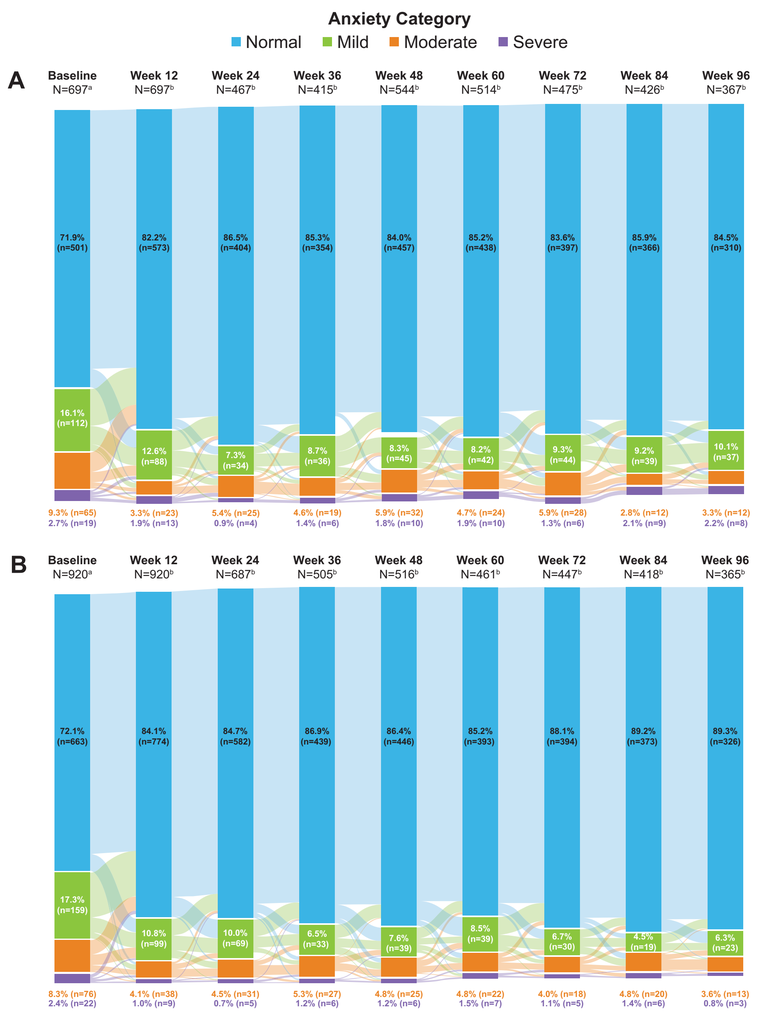


HADS-A, Hospital Anxiety and Depression Scale–Anxiety; HADS-D, Hospital Anxiety and Depression Scale–Depression.
HADS-A or HADS-D scores ranged from 0 to 21, with 0-7 representing normal, 8-10 mild, 11-14 moderate, and 15-21 severe levels of anxiety or depression.[8]

Changes in Anxiety and Depression Score Categories Over Time

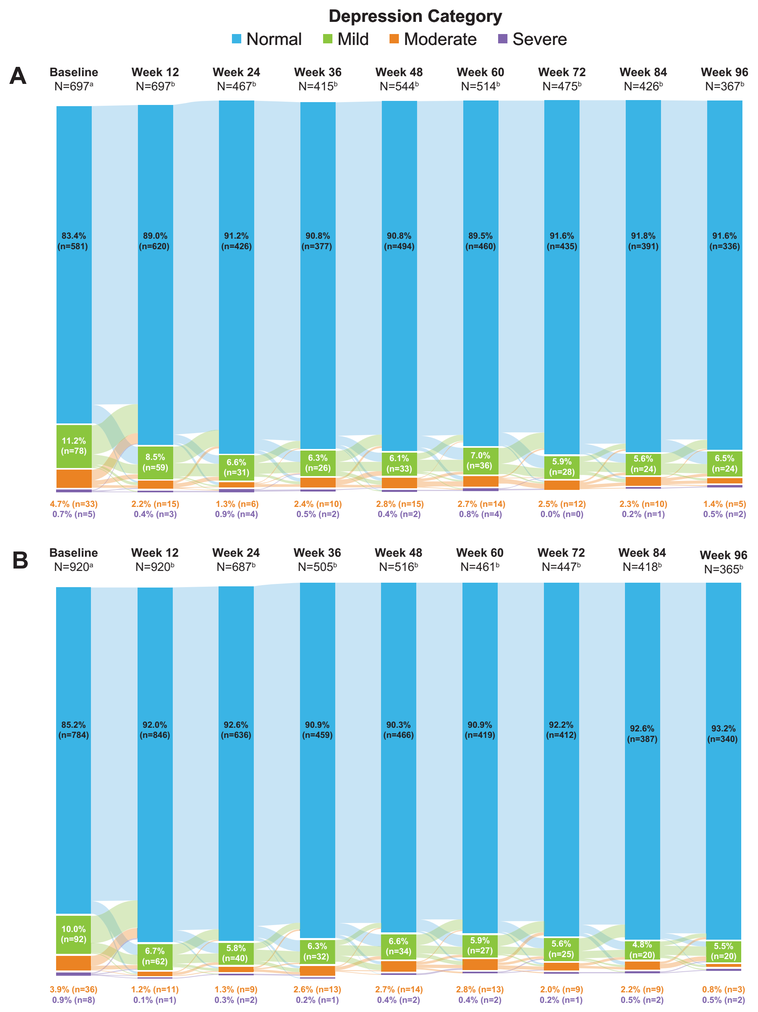
- The proportions of patients with mild, moderate, or severe anxiety or depression decreased from baseline to Week 12, with improvements observed through Week 96, while proportions of patients with HADS-A or HADS-D scores in the normal range increased with both abrocitinib 100 mg and abrocitinib 200 mg through Week 96 (**Figures 2** and **3**)
  - The largest shift observed in HADS-A and HADS-D categories was for patients with mild or moderate scores at baseline whose scores were classified as normal at Week 12 of abrocitinib treatment

Figure 2. Changes in HADS-A Score Categories Over Time in Patients Treated With (A) Abrocitinib 100 mg or (B) Abrocitinib 200 mg



HADS-A, Hospital Anxiety and Depression Scale–Anxiety.
JADE EXTEND is an ongoing study and not all patients had reached the Week 96 timepoint at the time of this analysis.
HADS-A scores range from 0 to 21, with 0-7 representing normal, 8-10 mild, 11-14 moderate, and 15-21 severe levels of anxiety.[8]
[a]Patients at study baseline with available data at both baseline and Week 12.
[b]Patients with available data at the previous and current time point.

Figure 3. Changes in HADS-D Score Categories Over Time in Patients Treated With (A) Abrocitinib 100 mg or (B) Abrocitinib 200 mg

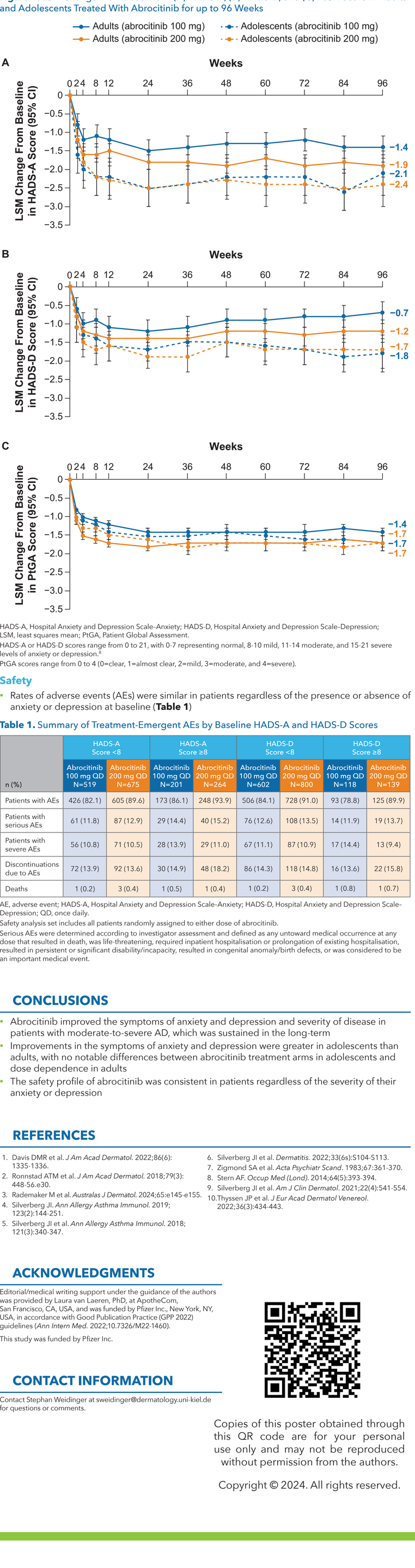


HADS-D, Hospital Anxiety and Depression Scale–Depression.
JADE EXTEND is an ongoing study and not all patients had reached the Week 96 timepoint at the time of this analysis.
HADS-D scores range from 0 to 21, with 0-7 representing normal, 8-10 mild, 11-14 moderate, and 15-21 severe levels of depression.[8]
[a]Patients at study baseline with available data at both baseline and Week 12.
[b]Patients with available data at both the previous and current time point.

Changes in Anxiety and Depression Scores Over Time

- In both adults and adolescents, LSM HADS-A and HADS-D scores decreased from baseline with abrocitinib treatment as early as Week 2 and reductions were sustained through Week 96; these observations were dose dependent in adult patients (**Figure 4A-B**)
  - Adolescent patients had greater improvements in both HADS-A and HADS-D scores than adult patients
- AD severity, as measured by PtGA scores, decreased with abrocitinib treatment as early as Week 2 and was sustained through Week 96; these observations were dose dependent in adult patients (**Figure 4C**)

Figure 4. LSM Change From Baseline in (A) HADS-A, (B) HADS-D, and (C) PtGA Score in Adults and Adolescents Treated With Abrocitinib for up to 96 Weeks



HADS-A, Hospital Anxiety and Depression Scale–Anxiety; HADS-D, Hospital Anxiety and Depression Scale–Depression; LSM, least squares mean; PtGA, Patient Global Assessment.
HADS-A or HADS-D scores range from 0 to 21, with 0-7 representing normal, 8-10 mild, 11-14 moderate, and 15-21 severe levels of anxiety or depression.[8]
PtGA scores range from 0 to 4 (0=clear, 1=almost clear, 2=mild, 3=moderate, and 4=severe).

Safety

- Rates of adverse events (AEs) were similar in patients regardless of the presence or absence of anxiety or depression at baseline (**Table 1**)

Table 1. Summary of Treatment-Emergent AEs by Baseline HADS-A and HADS-D Scores

n (%)	HADS-A Score <8		HADS-A Score ≥8		HADS-D Score <8		HADS-D Score ≥8	
	Abrocitinib 100 mg QD N=519	Abrocitinib 200 mg QD N=675	Abrocitinib 100 mg QD N=201	Abrocitinib 200 mg QD N=264	Abrocitinib 100 mg QD N=602	Abrocitinib 200 mg QD N=800	Abrocitinib 100 mg QD N=118	Abrocitinib 200 mg QD N=139
Patients with AEs	426 (82.1)	605 (89.6)	173 (86.1)	248 (93.9)	506 (84.1)	728 (91.0)	93 (78.8)	125 (89.9)
Patients with serious AEs	61 (11.8)	87 (12.9)	29 (14.4)	40 (15.2)	76 (12.6)	108 (13.5)	14 (11.9)	19 (13.7)
Patients with severe AEs	56 (10.8)	71 (10.5)	28 (13.9)	29 (11.0)	67 (11.1)	87 (10.9)	17 (14.4)	13 (9.4)
Discontinuations due to AEs	72 (13.9)	92 (13.6)	30 (14.9)	48 (18.2)	86 (14.3)	118 (14.8)	16 (13.6)	22 (15.8)
Deaths	1 (0.2)	3 (0.4)	1 (0.5)	1 (0.4)	1 (0.2)	3 (0.4)	1 (0.8)	1 (0.7)

AE, adverse event; HADS-A, Hospital Anxiety and Depression Scale-Anxiety; HADS-D, Hospital Anxiety and Depression Scale–Depression; QD, once daily.
Safety analysis set includes all patients randomly assigned to either dose of abrocitinib.
Serious AEs were determined according to investigator assessment and defined as any untoward medical occurrence at any dose that resulted in death, was life-threatening, required inpatient hospitalisation or prolongation of existing hospitalisation, resulted in persistent or significant disability/incapacity, resulted in congenital anomaly/birth defects, or was considered to be an important medical event.

CONCLUSIONS

- Abrocitinib improved the symptoms of anxiety and depression and severity of disease in patients with moderate-to-severe AD, which was sustained in the long-term
- Improvements in the symptoms of anxiety and depression were greater in adolescents than adults, with no notable differences between abrocitinib treatment arms in adolescents and dose dependence in adults
- The safety profile of abrocitinib was consistent in patients regardless of the severity of their anxiety or depression

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