Efficacy and safety of deuruxolitinib, an oral selective Janus kinase inhibitor, in adults with alopecia areata: Results from the Phase 3 randomized, controlled trial (THRIVE-AA1)

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Background: Alopecia areata (AA) is a hair loss disorder that can seriously impact quality of life. Janus kinase (JAK) inhibitors, including deuruxolitinib, have previously demonstrated significant hair regrowth in AA.

Objective: The Phase 3 THRIVE-AA1 randomized, double-blinded, placebo-controlled trial (NCT04518995) evaluated the safety and efficacy of the oral JAK1/JAK2 inhibitor deuruxolitinib in adult patients with AA.

Methods: Patients aged 18-65 years with ≥50% hair loss were randomized to deuruxolitinib 8 mg twice daily, deuruxolitinib 12 mg twice daily, or placebo for 24 weeks. The primary end point was the percentage of patients achieving a Severity of Alopecia Tool score ≤20. A key secondary end point was the percentage of satisfaction of hair patient-reported outcome responders.

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Patient consent: Consent for the publication of recognizable patient photographs was obtained by the authors and included at the time of article submission to the journal, stating that all patients gave consent with the understanding that this information may be publicly available for medical publication, presentation at a medical conference, and/or for teaching purposes.

IRB approval status: The study protocol and any amendments, the sponsor's approved informed consent form(s) (ICF), participant information sheets, participant recruitment materials, and other appropriate documents were submitted to each center's relevant IRB/EC for review and approval.

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Results: Significantly higher proportions of patients taking deuruxolitinib met the primary end point (8 mg 29.6%; 12 mg 41.5% versus placebo 0.8%). Both deuruxolitinib doses achieved significant improvements in all secondary end points versus placebo, including satisfaction of hair patient-reported outcome (8 mg 42.1%; 12 mg 53.0% versus placebo 4.7%). Most treatment-emergent adverse events were mild or moderate, consistent with other oral JAK inhibitors.

Limitations: Further studies are required to understand longer-term safety, efficacy, and impact of treatment cessation.

Conclusion: Both doses of deuruxolitinib were effective for hair regrowth. Patient satisfaction aligned with hair growth. (J Am Acad Dermatol 2024;91:880-8.)

Key words: alopecia areata; deuruxolitinib; Janus kinase (JAK) inhibitor; Phase 3; Severity of Alopecia Tool (SALT); THRIVE-AA1.

INTRODUCTION

Alopecia areata (AA) is an autoimmune disease causing nonscarring hair loss that is often patchy, but it may also lead to total scalp and body hair loss.[1] The disease is associated with anxiety and depression, as well as declines in social functioning and productivity, making it a daily challenge for many patients.[2,3]

CAPSULE SUMMARY

- Significant proportions of adult patients with alopecia areata and ≥50% scalp hair loss achieved ≤20% scalp hair loss during 24 weeks of treatment with deuruxolitinib versus placebo. Improvements in hair growth were reflected in patient hair satisfaction scores.
- Deuruxolitinib was well tolerated and effective, though longer-term studies are needed.

Prior to the recent indication of Janus kinase (JAK) inhibitors, there were no US Food and Drug Administration-approved therapies for AA. Treatments included topical, intralesional, or systemic corticosteroids,[1] as well as noncorticosteroid systemic immunosuppressive therapies, such as methotrexate and cyclosporine, and topical contact immunotherapy.[1] However, these treatments have shown variable efficacy and are based on limited evidence.[1,4-6] Consequently, there is an unmet need for more effective therapies.[1]

JAK inhibition has been the focus of current therapeutic strategies due to the involvement of interferon-γ and interleukin-15 in AA pathobiology, which signal through the JAK-signal transducer and activator of transcription pathway.[1,4,7] The JAK1/2 inhibitor baricitinib[8] and JAK3/tyrosine kinase expressed in hepatocellular carcinoma inhibitor ritlecitinib[9] are currently indicated for patients with severe AA. The JAK1/2 inhibitor deuruxolitinib (CTP-543) has also demonstrated significant dose-dependent increases in hair regrowth versus placebo in a Phase 2 clinical trial (NCT03137381).[10] Here, we report results from a Phase 3 randomized controlled trial, THRIVE-AA1 (NCT04518995), which evaluated the safety and efficacy of deuruxolitinib as a first-line treatment in adult patients with AA.

METHODS

Trial design and oversight

THRIVE-AA1 was a randomized, double-blinded, placebo-controlled trial conducted across 72 sites in the United States, Canada, and Europe between November 23, 2020, and April 19, 2022. It consisted of a 28-day screening period, a 24-week treatment period, and an optional open-label extension (OLE) (NCT03898479, NCT05041803) or 4-week posttreatment safety follow-up period (Supplementary Fig 1, available via Mendeley at https://data.mendeley.com/datasets/nmhhzwb96h/1). The study was conducted in accordance with the ethical principles of the Declaration of Helsinki and Good Clinical Practice guidelines. The protocol was approved by the central institutional review board or ethics committee at each site. CoNCERT Pharmaceuticals, Inc (subsequently acquired by Sun Pharmaceutical Industries Limited) designed, conducted blinded safety monitoring, analyzed the results, and also supplied deuruxolitinib and placebo. An independent data monitoring committee performed regular safety assessments.

Participants

Eligible participants were patients aged 18-65 years with ≥50% scalp hair loss (defined as a Severity of Alopecia Tool [SALT] score ≥50 at screening and baseline) and a current episode of scalp hair loss of AA lasting between 6 months and

Abbreviations used:

AA: alopecia areata
AE: adverse event
CI: confidence interval
JAK: Janus kinase
OLE: open-label extension
SALT: Severity of Alopecia Tool
SPRO: satisfaction of hair patient-reported outcome
TEAE: treatment-emergent adverse event

10 years at screening. Patients with a total disease duration >10 years were allowed. Exclusion criteria included recent treatment with medications/agents that could have affected hair regrowth or immune response, and patients with a known history of moderate to severe androgenic alopecia or female pattern hair loss (ie, hormonally driven AA as opposed to autoimmune). Full inclusion and exclusion criteria are available in the Supplementary Appendix, available via Mendeley at https://data.mendeley.com/datasets/nmhhzwb96h/1.

Study procedures

Patients were randomized in a 3:5:2 ratio to receive oral deuruxolitinib 12 mg twice daily, deuruxolitinib 8 mg twice daily, or placebo. Randomization was stratified by baseline scalp hair loss (partial [SALT 50-94] or complete/near-complete [SALT ≥95]) and performed using an interactive web-response system. Identical tablets and packaging were used for deuruxolitinib and placebo to maintain investigator and patient/caregiver blinding throughout the study. Individualized dose adjustment was not permitted during the treatment period.

Assessments

Trained raters measured the extent of hair loss using the SALT during in-person patient visits every 4 weeks, and there were photographic records of the scalp to monitor changes. SALT scores were not recorded for remote visits due to COVID-19 restrictions. The single-item satisfaction of hair patient-reported outcome (SPRO) question was also used to assess patient hair satisfaction, with possible scores ranging from very satisfied (1) to very dissatisfied (5). SPRO responders were defined as patients who answered very satisfied (1) or satisfied (2). Safety evaluations were performed regularly during the study, and adverse events (AEs) were coded according to the Medical Dictionary for Regulatory Activities, version 23.1.

End points

The primary efficacy end point was the percentage of patients who achieved a SALT score ≤20 at week 24. Key secondary end points were the percentage of SPRO responders at week 24 and patients with SALT score ≤20 at weeks 8, 12, 16, and 20 (week 8 being an amendment to the original protocol). Further secondary end points included patients achieving a SALT score ≤10 at week 24. Safety evaluations comprised AEs, clinical laboratory results, vital sign measurements, concomitant medications, and physical examinations.

Statistical analysis

Based on Phase 2 clinical trial results, the percentage of patients achieving a SALT score ≤20 at week 24 was assumed to be 40%, 25%, and 10% for the 12 mg twice daily, 8 mg twice daily, and placebo groups, respectively. This informed the 3:5:2 randomization ratio, for which a sample of ~700 patients gave >99% power to compare deuruxolitinib 12 mg twice daily and placebo and approximately 94% power to compare deuruxolitinib 8 mg twice daily and placebo, for the primary end point. A ≤ .025 (two-sided) alpha level was allocated to each dose for comparison with placebo for the primary and key secondary efficacy analyses to control for multiplicity of testing associated with 2 doses. Conditional upon significance of the primary and first key secondary end point, a gated, linear hierarchical (eg, step-wise) testing approach was used to test the remaining key secondary end points versus placebo ($P \leq .025$; Supplementary Fig 1, available via Mendeley at https://data.mendeley.com/datasets/nmhhzwb96h/1). For all other statistical tests outside this hierarchy, a two-sided significance level of ≤ .05 (ie, nominal P values without adjustment for multiple comparisons) was used. Pairwise treatment group differences from placebo for the proportions of patients with a SALT score ≤10 after 24 weeks were assessed using the Cochran-Mantel-Haenszel test, with baseline scalp hair loss as a stratification factor (partial versus complete/near complete). Missing values were included using multiple imputation under missing at random assumptions. All analyses were conducted using SAS, 9.4. Safety summaries were descriptive only. The efficacy population included all patients randomized and dispensed study drug, while the safety population comprised all patients receiving the study drug.

RESULTS

Participants

Enrollment began on November 23, 2020, with the last patient completing the study on April 19, 2022.

Table I. Baseline demographic and clinical characteristics (all randomized patients with AA)

Characteristic	Placebo (*n* = 140)	Deuruxolitinib 8 mg BID (*n* = 351)	Deuruxolitinib 12 mg BID (*n* = 215)
Demographic characteristic			
Median age, years (range)	38.5 (18-65)	37.0 (18-65)	36.0 (18-65)
Female sex, *n* (%)	89 (63.6)	217 (61.8)	131 (60.9)
Race, *n* (%)			
American Indian or Alaska native	0	2 (0.6)	1 (0.5)
Asian	10 (7.1)	22 (6.3)	21 (9.8)
Black or African American	16 (11.4)	40 (11.4)	27 (12.6)
Native Hawaiian or Pacific Islander	1 (0.7)	3 (0.9)	1 (0.5)
White	98 (70.0)	241 (68.7)	145 (67.4)
Other	5 (3.6)	17 (4.8)	6 (2.8)
Not applicable	10 (7.1)	26 (7.4)	14 (6.5)
Clinical characteristic			
Mean baseline SALT score (SD)	88.1 (15.10)	85.5 (18.35)	85.2 (18.41)
AA classification, *n* (%)			
Partial scalp hair loss (SALT ≥50 and <95)	62 (44.3)	155 (44.2)	95 (44.2)
Complete or near-complete scalp hair loss (SALT ≥95)	78 (55.7)	196 (55.8)	120 (55.8)
Median duration of current AA episode, years (range)	3.3 (1-10)	2.9 (1-11)	2.5 (0-11)
Current nail involvement, *n* (%)	53 (37.9)	116 (33.0)	74 (34.4)
Current nasal hair involvement, *n* (%)	87 (62.1)	180 (51.3)	124 (57.7)
Current eyebrow involvement, *n* (%)	97 (69.3)	245 (69.8)	151 (70.2)
Current eyelash involvement, *n* (%)	92 (65.7)	246 (70.1)	158 (73.5)

AA, Alopecia areata; *BID*, twice daily; *SALT*, Severity of Alopecia Tool; *SD*, standard deviation.

Overall, 706 patients were randomized to deuruxolitinib 8 mg twice daily (n = 351), deuruxolitinib 12 mg twice daily (n = 215), or placebo (n = 140), and 705 received the study drug (Supplementary Fig 2, available via Mendeley at https://data.mendeley.com/datasets/nmhhzwb96h/1), comprising the efficacy and safety populations, respectively. Treatment was completed by 316/351 (90.0%), 197/215 (91.6%), and 129/140 (92.1%) of patients in the 8 mg twice daily, 12 mg twice daily, and placebo groups, respectively. Across all groups, patients were median 37.0 years old (range: 18-65), 61.9% female, and 68.6% White. Baseline demographics and clinical characteristics were well balanced across groups (Table I). The median (range) duration of the current AA episode was 2.8 years (0-11) for all patients, with a mean baseline SALT score of 85.9 (standard deviation ± 17.78).

Primary efficacy outcome

Both doses of deuruxolitinib led to significantly higher proportions of patients achieving a SALT score ≤20 after 24 weeks versus placebo; 94 (29.6%) and 83 (41.5%) patients with complete data in the 8 mg twice daily and 12 mg twice daily groups, respectively, and one (0.8%) patient in the placebo group (Fig 1). The Mantel-Haenszel common risk difference estimated with multiple imputation for missing data was 0.28 (95% confidence interval [CI]: 0.23, 0.33; $P < .0001$) for 8 mg twice daily and 0.39 (95% CI: 0.32, 0.46; $P < .0001$) for 12 mg twice daily versus placebo. Stratified by baseline scalp hair loss, 57/134 (42.5%), 50/88 (56.8%), and 1/55 (1.8%) of patients with partial hair loss in the 8 mg twice daily, 12 mg twice daily, and placebo groups, respectively, achieved a SALT score ≤20 at week 24, compared with 37/184 (20.1%), 33/112 (29.5), and 0/73 (0%) in patients with complete or near-complete hair loss. Photographic representation of hair regrowth after 24 weeks is shown in Supplementary Fig 3, available via Mendeley at https://data.mendeley.com/datasets/nmhhzwb96h/1.

Key secondary efficacy outcomes

Aligned with the primary end point, both doses of deuruxolitinib resulted in significant improvements in all key secondary outcomes versus placebo. At week 24, SPRO responders were observed in 42.1% and 53.0% of patients in the 8 mg twice daily and 12 mg twice daily groups, respectively, versus 4.7% in the placebo group (Fig 2). The Mantel-Haenszel common risk difference estimated with multiple imputation for missing data was 0.38 (95% CI: 0.31, 0.44; $P < .0001$) for 8 mg twice daily and 0.47 (95% CI: 0.39, 0.55; $P < .0001$) for 12 mg twice daily versus placebo.

Significantly higher proportions of patients receiving deuruxolitinib achieved a SALT score ≤20 after 8, 12, 16, and 20 weeks versus placebo (Fig 1).

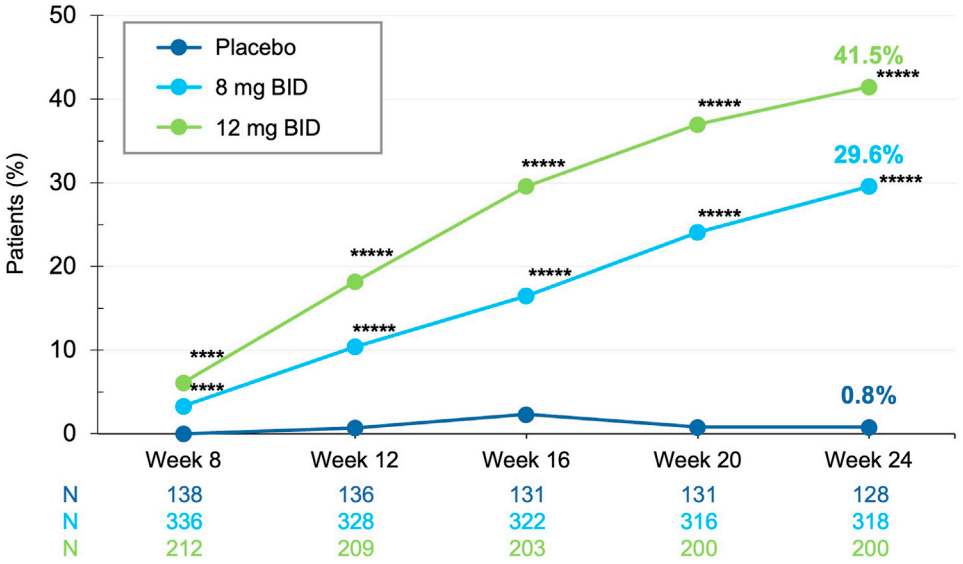

Fig 1. Percentage of patients with AA achieving a SALT score ≤20 throughout the treatment period. ****$P \leq .001$ vs placebo; *****$P \leq .0001$ vs placebo. Percentages were based on observed data. *P* values were based on the Mantel-Haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared with placebo. *N* values represent the number of patients with available data at each time point. Missing values were imputed using multiple imputation under missing at random assumptions. Responders were patients with a SALT score ≤20. *AA*, Alopecia areata; *BID*, twice daily; *SALT*, Severity of Alopecia Tool.

The proportions of patients achieving a SALT score ≤10 after 24 weeks were also significantly higher in the 8 mg twice daily (20.8%) and 12 mg twice daily (34.5%) groups versus placebo (0%) (Fig 3).

Safety

Treatment-emergent adverse events (TEAEs; Table II) were reported by 65.1% and 63.7% of patients in the 8 mg twice daily and 12 mg twice daily groups, respectively, and 55.7% in the placebo group. Most were mild to moderate in severity. TEAEs considered related to the study drug were reported by 31.1% and 34.9% in the 8 mg twice daily and 12 mg twice daily groups, respectively, and 22.1% in the placebo group (Supplementary Table I, available via Mendeley at https://data.mendeley.com/datasets/nmhhzwb96h/1).

During the study, serious TEAEs occurred in 1.1% and 0.5% of 8 mg twice daily and 12 mg twice daily patients, respectively, and 2.9% of placebo patients. Two serious TEAEs, pyrexia and meningitis, were considered related to the study drug and occurred in a single patient receiving deuruxolitinib 8 mg twice daily, leading to study drug interruption, but subsequently resolved. Notably, the patient had a spinal cord stimulator implanted and spinal injection 1 day prior to these serious TEAEs. No deaths occurred during the study.

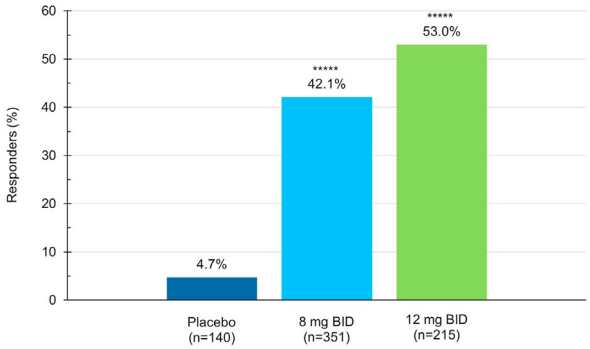

Fig 2. Percentage of patients with AA reporting a response of "very satisfied" or "satisfied" according to SPRO at week 24. *****$P < .0001$ vs placebo. Percentages were based on observed data. *P* values were based on the Mantel-Haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared with placebo. Missing values were imputed using multiple imputation under missing at random assumptions. Responders were defined as patients with responses of "very satisfied" or "satisfied." *AA*, Alopecia areata; *BID*, twice daily; *SPRO*, satisfaction of hair patient-reported outcome.

TEAEs causing study drug discontinuation were more frequent in deuruxolitinib 8 mg twice daily and 12 mg twice daily groups (2.6% and 2.8%, respectively) versus placebo (1.4%) (Supplementary Table II, available via Mendeley at https://data.mendeley.com/

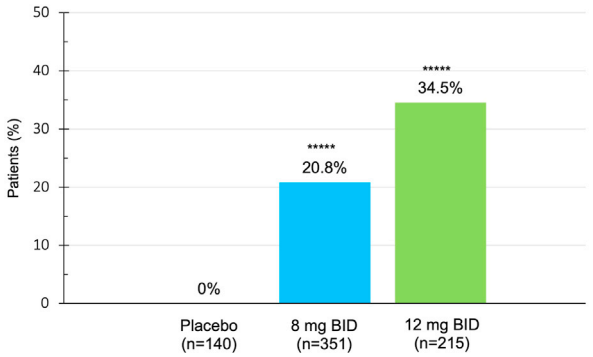

Fig 3. Percentage of patients with AA achieving a SALT score ≤10 at week 24. *****$P \leq .0001$ vs placebo. Percentages were based on observed data. *P* values were based on the Mantel-Haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared with placebo. Missing values were imputed using multiple imputation under missing at random assumptions. *AA*, Alopecia areata; *BID*, twice daily; *SALT*, Severity of Alopecia Tool.

datasets/nmhhzwb96h/1). TEAEs leading to study drug interruption were reported in 8.6%, 10.7%, and 6.4% of patients in 8 mg twice daily, 12 mg twice daily, and placebo groups, respectively (Supplementary Table III, available via Mendeley at https://data.mendeley.com/datasets/nmhhzwb96h/1).

Except for a trend of higher weight gain (mean change from baseline 1.27 kg and 1.78 kg for 8 mg twice daily and 12 mg twice daily, respectively, versus placebo 0.23 kg), no clinically meaningful changes were observed in vital signs or electrocardiogram results. Two cases of herpes zoster occurred during the study, one in each of the 8 mg twice daily and 12 mg twice daily groups, which resolved without dose interruptions. No myocardial infarctions, strokes, malignancies, or thromboembolic events were reported in patients receiving deuruxolitinib.

Although changes in some laboratory parameters were observed with deuruxolitinib treatment (Supplementary Table IV, available via Mendeley at https://data.mendeley.com/datasets/nmhhzwb96h/1), they were mostly not clinically significant. Grade 3 or 4 low neutrophil count occurred in 1.7%, 2.8%, and 0.7% of patients in the 8 mg twice daily, 12 mg twice daily, and placebo groups, respectively. No symptomatic anemia was observed, although one patient in the 12 mg twice daily group discontinued treatment due to anemia. Mean baseline platelet counts were 264.2×10^9/L, 255.9×10^9/L, and 264.0×10^9/L in the 8 mg twice daily, 12 mg twice daily, and placebo groups, respectively, with maximum postbaseline values of 371.5×10^9/L, 386.1×10^9/L, and 286.3×10^9/L, respectively. Increases in mean platelet counts with corresponding decreases in mean platelet volumes were observed in both deuruxolitinib groups, which may reflect an increase in circulating platelet age during treatment. The increase in platelet count was seen at week 2 and plateaued thereafter. No bleeding, bruising, or clotting abnormalities were associated with abnormal platelet counts.

Three patients in the 8 mg twice daily group discontinued due to elevated platelet count. Mean blood creatine phosphokinase levels were elevated in the deuruxolitinib groups versus placebo, as expected for this class of drugs. Grade 3 or 4 changes in serum chemistry parameters included elevated creatine phosphokinase, lipase, potassium, aspartate aminotransferase, and amylase, as well as low sodium; all of which were asymptomatic. No cases of rhabdomyolysis occurred. A small number of patients had grade 3 elevations in triglycerides and cholesterol. One patient in the 8 mg twice daily group discontinued the study drug due to grade 4 lipase elevation.

DISCUSSION

Treatment with deuruxolitinib 8 mg twice daily and 12 mg twice daily led to a SALT score ≤20 after 24 weeks in 29.6% and 41.5% of patients, respectively. Statistically significant hair regrowth versus placebo in both dose groups was observed as early as week 8. Patient satisfaction with scalp hair growth corroborated clinician assessments. Most patients who achieved primary efficacy outcomes also achieved a SALT score ≤10 after 24 weeks. These results, as well as the efficacy of the previously approved JAK inhibitors, baricitinib, and ritlecitinib,[11,12] provide support for JAK inhibition as a treatment strategy in AA.

Deuruxolitinib had a similar incidence of AEs across groups and was generally well tolerated. Headache, acne, and increased blood creatine phosphokinase occurred in ≥5% of patients in both deuruxolitinib groups, while serious AEs were uncommon (and only 2 were considered by the study investigator to be potentially related to the study drug). Few treatment discontinuations occurred due to AEs, and no myocardial infarction, stroke, or thromboembolic events occurred. Herpes zoster was rare.

Limitations included the relatively short duration of the double-blinded period, as the proportions of patients achieving a SALT score ≤20 did not plateau, and longer-term efficacy and safety of deuruxolitinib require further study. To address this, 633/642

Table II. Summary of key safety outcomes in patients with AA during the 24-week study period

Outcome	Placebo (*n* = 140)	Deuruxolitinib 8 mg BID (*n* = 350)	Deuruxolitinib 12 mg BID (*n* = 215)
Patients with ≥1 TEAE, *n* (%)	78 (55.7)	228 (65.1)	137 (63.7)
Mild	67 (47.9)	188 (53.7)	118 (54.9)
Moderate	22 (15.7)	92 (26.3)	58 (27.0)
Severe	4 (2.9)	7 (2.0)	4 (1.9)
Patients with ≥1 treatment-related TEAE, *n* (%)*	31 (22.1)	109 (31.1)	75 (34.9)
Possibly related	27 (19.3)	84 (24.0)	44 (20.5)
Probably related	9 (6.4)	34 (9.7)	29 (13.5)
Definitely related	1 (0.7)	12 (3.4)	13 (6.0)
Serious TEAEs, *n* (%)	4 (2.9)	4 (1.1)	1 (0.5)
Patients with ≥1 TEAE leading to study drug interruption, *n* (%)	9 (6.4)	30 (8.6)	23 (10.7)
Patients with ≥1 TEAE leading to study drug discontinuation, *n* (%)	2 (1.4)	9 (2.6)	6 (2.8)
Death, *n*	0	0	0
TEAEs occurring in ≥2% of patients in any group, *n* (%)			
Infections and infestations			
COVID-19	8 (5.7)	19 (5.4)	15 (7.0)
Nasopharyngitis	5 (3.6)	18 (5.1)	8 (3.7)
Upper respiratory tract infection	9 (6.4)	9 (2.6)	8 (3.7)
Urinary tract infection	3 (2.1)	7 (2.0)	4 (1.9)
Sinusitis	0	9 (2.6)	3 (1.4)
Influenza	3 (2.1)	0	0
Investigations			
Increased blood creatine phosphokinase	2 (1.4)	21 (6.0)	11 (5.1)
Increased weight	2 (1.4)	7 (2.0)	5 (2.3)
Increased cholesterol	3 (2.1)	4 (1.1)	6 (2.8)
Increased platelet count	0	8 (2.3)	3 (1.4)
Increased HDL	2 (1.4)	3 (0.9)	5 (2.3)
Nervous system disorders			
Headache	8 (5.7)	41 (11.7)	24 (11.2)
Skin and subcutaneous tissue disorders			
Acne	7 (5.0)	31 (8.9)	26 (12.1)
Contact dermatitis	3 (2.1)	2 (0.6)	2 (0.9)
Pruritus	3 (2.1)	3 (0.9)	1 (0.5)
Gastrointestinal disorders			
Diarrhea	3 (2.1)	5 (1.4)	9 (4.2)
Nausea	1 (0.7)	8 (2.3)	5 (2.3)
General disorders and administration site conditions			
Fatigue	2 (1.4)	6 (1.7)	7 (3.3)
Pyrexia	3 (2.1)	5 (1.4)	1 (0.5)
Injury, poisoning, and procedural complications			
Vaccination complication	1 (0.7)	3 (0.9)	5 (2.3)
Musculoskeletal and connective tissue disorders			
Arthralgia	6 (4.3)	4 (1.1)	1 (0.5)
Respiratory, thoracic, and mediastinal disorders			
Cough	3 (2.1)	2 (0.6)	2 (0.9)
Oropharyngeal pain	3 (2.1)	3 (0.9)	0
Blood and lymphatic system disorders			
Anemia	0	4 (1.1)	5 (2.3)
TEAEs of special interest, *n* (%)			
Infections	31 (22.1)	83 (23.7)	63 (29.3)
Herpes zoster	0	1 (0.3)	1 (0.5)
Deep vein thrombosis	0	0	0

Continued

Table II. Cont'd

Outcome	Placebo (n = 140)	Deuruxolitinib 8 mg BID (n = 350)	Deuruxolitinib 12 mg BID (n = 215)
Malignancy	0	0	0
Gastrointestinal perforation	0	0	0
Myocardial infarction	0	0	0
Pulmonary embolism	0	0	0
Stroke	0	0	0

AA, Alopecia areata; *BID*, twice daily; *HDL*, high-density lipoprotein; *TEAE*, treatment-emergent adverse event.
*Patients were counted once for any relation, then once for each category of relatedness.

(98.6%) of eligible patients completing this study have entered an OLE. Notably, although no thromboembolic events occurred in the double-blinded period of this study, 5 potentially study-drug-related cases have been reported in patients during the long-term OLE studies (8 mg twice daily [n = 1]; 12 mg twice daily [n = 4]), including 3 cases of pulmonary embolism (all 12 mg twice daily). Consequently, the 12 mg twice daily dose has been discontinued from these ongoing OLE studies. Durability of hair regrowth was not assessed during the study, and it will be important to assess AA recurrence following treatment cessation.[4,13] As remote visits due to COVID-19 restrictions were only carried out in a small number of patients (Supplementary Table V, available via Mendeley at https://data.mendeley.com/datasets/nmhhzwb96h/1) and no SALT assessments were carried out remotely, this did not impact the study conduct or data integrity.

In conclusion, treatment with deuruxolitinib resulted in significant scalp hair growth as early as 8 weeks, which continued throughout the 24-week study period, with patient satisfaction reflecting the hair regrowth observed. In addition, deuruxolitinib was generally well tolerated. Analyses of efficacy and safety over longer treatment periods are underway.

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Conflicts of interest

Dr King has served on advisory boards and/or is a consultant and/or is a clinical trial investigator for AbbVie, AltruBio Inc, Almirall, AnaptysBio, Arena Pharmaceuticals, Bioniz Therapeutics, Bristol Myers Squibb, CoNCERT Pharmaceuticals (subsequently acquired by Sun Pharmaceutical Industries Limited), Equillium, Horizon Therapeutics, Eli Lilly, Incyte Corp., Janssen Pharmaceuticals, LEO Pharma, Otsuka/Visterra Inc, Pfizer, Regeneron, Sanofi Genzyme, Sun Pharmaceutical Industries Limited, TWi Biotechnology Inc, and Viela Bio Inc; also served on speaker bureaus for AbbVie, Incyte, Eli Lilly, Pfizer, Regeneron, and Sanofi Genzyme and is a scientific advisor for BiologicsMD. Dr Senna has been a speaker for Eli Lilly and Pfizer and a principal investigator and/or received research funding from Follica, Eli Lilly, CoNCERT Pharmaceuticals (subsequently acquired by Sun Pharmaceutical Industries Limited), Santiste Medical, and LEO Pharma; has also served on scientific advisory boards and/or been a consultant for Eli Lilly, Follica, L'Oreal, Kintor, and Pfizer, and is on the board of directors/medical advisory board for the National Alopecia Areata Foundation, Scarring Alopecia Foundation, and the American Hair Research Society. Dr Mesinkovska has been an advisor for CoNCERT Pharmaceuticals (subsequently acquired by Sun Pharmaceutical Industries Limited), Eli Lilly, and Pfizer, a principal investigator for AbbVie, Arcutis Biotherapeutics, Bristol Myers Squibb, CoNCERT Pharmaceuticals (subsequently acquired by Sun Pharmaceutical Industries Limited), Eli Lilly, and Pfizer and a speaker for Eli Lilly. Dr Lynde has been a speaker and/or consultant for AbbVie, Amgen, Aralez, Arcutis, Bausch Health, Bayer, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Cipher, Dermavant, Devonian, Eli Lilly, Fresenius Kabi, Galderma, GSK, Incyte, Innovaderm, Intega Skin, Janssen, Kyowa Kirin, La Roche Posay, LEO Pharma, L'Oreal, Medexus, MedX, Merck, Novartis, P&G, Pediapharm, Pfizer, Regeneron, Roche, Sanofi Genzyme, Sandoz, Sentrex, Sun Pharmaceutical Industries Limited, TEVA, Tribute, UCB, Viatris, and Volo Health; and has also been a principal investigator for AbbVie, Acelyrin, Akros, Altius, Amgen, Aralez, Arcutis, Avillion, Bausch Health, Bayer, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Celltrion, Cipher, CoNCERT Pharmaceuticals (subsequently acquired by Sun Pharmaceutical Industries Limited), Dermavant, Devonian, Eli Lilly, Evelo, Galderma, GSK, Incyte, Innovaderm, Intega Skin, Janssen, Kyowa Kirin, La Roche Posay, LEO Pharma, L'Oreal, Medexus, MedX, Merck, MoonLake, Novartis, P&G, Pediapharm, Pfizer, Regeneron, Roche, Sanofi Genzyme, Sandoz, Sentrex, Sun Pharmaceutical Industries Limited, TEVA, Tribute, UCB, Valeant, Viatris, and Volo Health. Dr Zirwas has been an investigator and/or speaker and/or consultant for AbbVie, Acrotech, Aldeyra, Advanced Derm Solutions, All Free Clear/Sun, Amgen, Anaptys Bio, Apogee, Arcutis, Bausch and Lomb, Biocon, Bristol Myers Squibb,

Cara, Castle Biosciences, CoNCERT Pharmaceuticals (subsequently acquired by Sun Pharmaceutical Industries Limited), Connect Biopharma, Dermavant, Edessa Biotech, EPI Health, Evelo, Galderma, Genentech/Novartis, Incyte, Janssen, L'Oreal, LEO Pharma, Level-Ex, Eli Lilly, LUUM, Nimbus, Oculus, Peloton, Pfizer, Regeneron/Sanofi, Trevi, Trifecta, and UCB; has also been an advisor for Vial and is part owner of AsepticMD. Dr Maari has served on advisory boards and/or is a consultant and/or is a clinical trial investigator for AbbVie, Almirall, AnaptysBio, Arena Pharmaceuticals, Bristol Myers Squibb, CoNCERT Pharmaceuticals (subsequently acquired by Sun Pharmaceutical Industries Limited), Horizon Therapeutics, Eli Lilly, Incyte Corp., Janssen Pharmaceuticals, LEO Pharma, Pfizer, Regeneron, Sanofi Genzyme, Sun Pharmaceutical Industries Limited, Valeant, Dermavant, Novartis, Amgen, and UCB. Dr Prajapati has been an advisor, consultant, and/or speaker for AbbVie, Actelion, Amgen, Aralez, Arcutis, Aspen, Bausch Health, BioScript Solutions, Boehringer Ingelheim, Bristol Myers Squibb, Canadian Psoriasis Network, Celgene, Cipher, CoNCERT Pharmaceuticals (subsequently acquired by Sun Pharmaceutical Industries Limited), CorEvitas, Eczema Society of Canada, Eli Lilly, Galderma, GlaxoSmithKline, Homeocan, Incyte, Janssen, LEO Pharma, Medexus, Novartis, Pediapharm, Pfizer, Sanofi Genzyme, Sun Pharmaceutical Industries Limited, Tribute, UCB, and Valeant; investigator for AbbVie, AnaptysBio, Arcutis, Arena, Bausch Health, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, CoNCERT Pharmaceuticals (subsequently acquired by Sun Pharmaceutical Industries Limited), CorEvitas, Dermavant, Dermira, Eli Lilly, Galderma, Incyte, Janssen, LEO Pharma, Nimbus Lakshmi, Novartis, Pfizer, RAPT Therapeutics, Regeneron, Reistone, Sanofi Genzyme, Takeda, and UCB; received grants from AbbVie, Bausch Health, Janssen, LEO Pharma, Novartis, and Sanofi Genzyme. Dr Sapra has been a principal investigator, consultant, or speaker for AbbVie, Amgen, Arcutis, Avillion, Bausch Health, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, CoNCERT Pharmaceuticals (subsequently acquired by Sun Pharmaceutical Industries Limited), Dermavant, Eli Lilly, Galderma, GSK, Incyte, Innovaderm, Janssen, LEO Pharma, Merz, Novartis, Pfizer, Pulse Biosciences, Regeneron, Roche, Sanofi, UCB, and Valeant. Dr Brzewski has been a principal investigator and/or consultant for AbbVie, Acelyrin, Alvotech Swiss, Amgen, BenevolentAI, Bioeq GmbH, Biogen, Celltrion, CoNCERT Pharmaceuticals (subsequently acquired by Sun Pharmaceutical Industries Limited), Eli Lilly, Horizon Therapeutics, Janssen, LEO Pharma, Pfizer, Regeneron, and Samsung Bioepis. Dr Osman has been an advisor for AbbVie, Affibody, Allergan, Amgen, AnaptysBio, Arcutis, Aurigene, Botanix, Castle Biosciences, Chemocentryx, CoNCERT Pharmaceuticals (subsequently acquired by Sun Pharmaceutical Industries Limited), Dermavant, DS Biopharma, Eli Lilly, Foamix Pharmaceuticals, Galderma, Janssen, Incyte, LEO Pharma, Reistone, Sun Pharmaceutical Industries Limited, and Valeant. Dr Hanna has been an advisory board member, principal investigator, investigator, speaker, and/or consultant for AbbVie, Akros, Allergan, Altius Healthcare, Amgen, Aralez, Arcutis, Bausch Health, Biopharma, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Coherus, CoNCERT Pharmaceuticals (subsequently acquired by Sun Pharmaceutical Industries Limited), Cutanea, Dermira, Galapagos, Galderma, Glenmark, Incyte, Janssen, LEO Pharma, Lilly, Lumenis, Merz, Novartis, Pediapharma, Pfizer, Prollenium, Regeneron, Revanesse, Reistone, Sandoz, Sanofi, Sun Pharma, and UCB. Dr Wiseman has been a principal investigator, consultant, advisor, or speaker for Acelyrin, AbbVie (previously Abbott), Akros, Amgen, Arcutis, Asana BioSciences, AstraZeneca, Bausch Health, Bristol Myers Squibb, CoNCERT Pharmaceuticals (subsequently acquired by Sun Pharmaceutical Industries Limited), Celgene, Dermavant, Dermira, Dice, Eli Lilly, Evelo, Galderma, Glenmark, Incyte, Janssen, LEO Pharma A/S, L'Oreal, Merck Frosst Canada, Moonlake, Novartis, Pfizer, Principia, PRCL Research, Regeneron, Sanofi, Takeda, Timber. Drs Hamilton and Cassella are employees of Sun Pharmaceutical Industries, Inc.

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