Safety assessments in the multinational Phase 3 THRIVE-AA1 trial with CTP-543 (deuruxolitinib) in adult patients with alopecia areata

Brett King[1], Natasha A Mesinkovska[2], Maryanne Makredes Senna[3], Arash Mostaghimi[4], Colleen Hamilton[5], James Cassella[5]

[1]Department of Dermatology, Yale School of Medicine, New Haven, CT, USA; [2]Department of Dermatology, University of California, Irvine, CA, USA; [3]Lahey Hair Loss Center of Excellence/Research Unit, Beth Israel Deaconess Medical Center, Burlington, MA, USA; [4]Department of Dermatology, Brigham and Women's Hospital, Boston, MA, USA; [5]Sun Pharmaceutical Industries, Inc., Lexington, MA, USA

INTRODUCTION

- Alopecia areata (AA) is an autoimmune disorder that causes partial or complete loss of hair, leading to reduced quality of life and considerable psychosocial impacts for patients[1]
- Janus kinase (JAK) inhibitors have been shown to reverse hair loss in patients with AA[2]
- Deuruxolitinib is an inhibitor of JAK1 and JAK2 that resulted in significant improvements in hair regrowth compared with placebo in the Phase 2 dose-ranging trial (NCT03137381)[3]

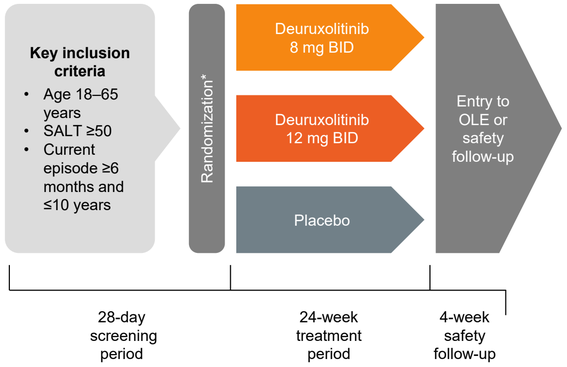
OBJECTIVE

- To present key safety outcomes from the randomized, controlled, Phase 3 THRIVE-AA1 trial in patients with AA (NCT04518995)

METHODS

- Eligible patients—adults (18–65 years of age) diagnosed with AA with ≥50% scalp hair loss—were randomized in a 3:5:2 ratio to receive deuruxolitinib 12 mg twice daily (BID), deuruxolitinib 8 mg BID, or placebo for 24 weeks (**Figure 1**)
- Safety assessments included adverse events (AEs), vital signs, electrocardiogram (ECG) results, and clinical laboratory tests

Figure 1. Study design



*Randomization 3:5:2 to deuruxolitinib 12 mg BID, deuruxolitinib 8 mg BID, or placebo. BID, twice daily; OLE, open-label extension; SALT, Severity of Alopecia Tool.

RESULTS

Table 1. Baseline demographics and disease characteristics

	Placebo (n = 140)	Deuruxolitinib 8 mg BID (n = 351)	Deuruxolitinib 12 mg BID (n = 215)	Total (N = 706)
Age, years, median (range)	38.5 (18–65)	37.0 (18–65)	36.0 (18–65)	37.0 (18–65)
Female, n (%)	89 (63.6)	217 (61.8)	131 (60.9)	437 (61.9)
White, n (%)	98 (70.0)	241 (68.7)	145 (67.4)	484 (68.6)
Duration of current episode, years, mean ± SD	3.9 ± 2.88	3.6 ± 2.63	3.6 ± 2.86	3.7 ± 2.75
Total SALT score, mean ± SD	88.1 ± 15.10	85.5 ± 18.35	85.2 ± 18.41	85.9 ± 17.78

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

- Most treatment-emergent AEs (TEAEs) were mild to moderate in severity (**Table 2**)
- Only 1 patient (deuruxolitinib 8 mg BID) reported serious AEs (SAEs) assessed as possibly related to treatment (pyrexia and spinal meningitis)
- The TEAEs resulting in discontinuation in >1 patient were headache and increased platelet count

Table 2. Summary of TEAEs through Week 24

	Placebo (n = 140)	Deuruxolitinib 8 mg BID (n = 350)	Deuruxolitinib 12 mg BID (n = 215)	Total (N = 705)
Patients with ≥1 TEAE	78 (55.7)	228 (65.1)	137 (63.7)	443 (62.8)
Patients with serious TEAEs	4 (2.9)	4 (1.1)	1 (0.5)	9 (1.3)
Related events, n	0	2[a]	0	2
Patients with related serious TEAEs	0	1 (0.3)	0	1 (0.1)
TEAEs leading to study drug discontinuation	2 (1.4)	9 (2.6)	6 (2.8)	17 (2.4)

Data are presented as n (%) unless otherwise indicated. [a]Drug was interrupted and the patient recovered; of note, the patient had a pain stimulator implanted and a spinal injection 1 day prior to reporting the serious adverse events.
BID, twice daily; TEAE, treatment-emergent adverse event.

- The most common TEAEs (≥5% of patients in any group) are shown in **Table 3**

Table 3. Most common TEAEs through Week 24

	Placebo (n = 140)	Deuruxolitinib 8 mg BID (n = 350)	Deuruxolitinib 12 mg BID (n = 215)	Total (N = 705)
Headache	8 (5.7)	41 (11.7)	24 (11.2)	73 (10.4)
Acne	7 (5.0)	31 (8.9)	26 (12.1)	64 (9.1)
COVID-19	8 (5.7)	19 (5.4)	15 (7.0)	42 (6.0)
Increase in blood creatine phosphokinase	2 (1.4)	21 (6.0)	11 (5.1)	34 (4.8)
Nasopharyngitis	5 (3.6)	18 (5.1)	8 (3.7)	31 (4.4)
Upper respiratory tract infection	9 (6.4)	9 (2.6)	8 (3.7)	26 (3.7)

Data are presented as n (%). BID, twice daily; COVID-19, coronavirus disease 2019; TEAE, treatment-emergent adverse event.

- Overall, 0.7% of patients (5/705) reported serious infections (AEs of special interest)
  - Appendicitis (3 cases; 1 in each treatment group, including placebo), coronavirus disease 2019 (COVID-19; 1 case in the 8-mg BID group), and meningitis (1 case in the 8-mg BID group)
  - Herpes zoster (2 cases; 1 in the deuruxolitinib 8-mg BID group and 1 in the deuruxolitinib 12-mg BID group); neither case was considered related to study drug, no dose interruptions occurred, and both cases recovered/resolved
- There were no thromboembolic events (deep vein thromboses [DVTs] or pulmonary embolisms [PEs]) or deaths during the observation period of this study
- Potentially significant clinical laboratory abnormalities occurring in ≥1% of patients are shown in **Table 4**
  - No symptomatic anemia or neutropenia-associated fevers/infections were observed

Table 4. Potentially clinically significant laboratory abnormalities in ≥1% of patients*

	Placebo (n = 140)	Deuruxolitinib 8 mg BID (n = 350)	Deuruxolitinib 12 mg BID (n = 215)
Neutropenia	1 (0.7)	6 (1.7)	6 (2.8)
Lymphopenia	0	4 (1.1)	3 (1.4)
Creatine kinase elevation	6 (4.3)	24 (6.9)	18 (8.5)
Lipase	3 (2.1)	10 (2.9)	6 (2.8)
Potassium	2 (1.4)	1 (0.3)	1 (0.5)
High triglycerides	0	5 (1.4)	1 (0.5)

Data are presented as n (%). *In any treatment group; defined as Grade 3 or 4 based on CTCAE criteria. Potentially significant clinical laboratory abnormalities in <1% of patients in any group included changes in sodium (0%, 0.6%, 0.5%), AST (0%, 0.3%, 0%), amylase (0.7%, 0%, 0%), and high cholesterol (0%, 0.3%, 0%) for placebo, deuruxolitinib 8 mg BID, and deuruxolitinib 12 mg BID, respectively. AST, aspartate aminotransferase; BID, twice daily; CTCAE, Common Terminology Criteria for Adverse Events.

CONCLUSIONS

- Deuruxolitinib was generally well tolerated at both the 8-mg BID and 12-mg BID doses
  - Most TEAEs (>95%) were mild to moderate in severity
  - Serious TEAEs were uncommon
  - Treatment discontinuations due to TEAEs were uncommon
  - Herpes zoster was rare
- No thromboembolic events (DVTs/PEs) or deaths were observed
- Changes in laboratory parameters were generally consistent with those previously observed for JAK inhibitors[4] and were not associated with clinical signs and symptoms
- The long-term safety profile will be evaluated in the ongoing open-label extension trials (NCT03898479 and NCT05041803)

REFERENCES

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DISCLOSURES

BK has been a consultant and/or scientific adviser and/or has served as a principal investigator for AbbVie, AltruBio Inc, Almirall, AnaptysBio, Arena Pharmaceuticals, Bioniz Therapeutics, Bristol Myers Squibb, CoNCERT Pharmaceuticals (acquired by Sun Pharma in March 2023), Eli Lilly, Equillium, Horizon Therapeutics plc, Incyte, Janssen, LEO Pharma, Otsuka/Visterra Inc, Pfizer, Regeneron, Sanofi Genzyme, Sun Pharma, TWi Biotechnology Inc, and Viela Bio; and has served as a speaker for AbbVie, Eli Lilly, Incyte, Pfizer, Regeneron, and Sanofi Genzyme; and as a scientific adviser for BiologicsMD. **NAM** has served as an adviser for CoNCERT Pharmaceuticals (acquired by Sun Pharma in March 2023), Eli Lilly, and Pfizer; as a principal investigator for AbbVie, Arcutis Biotherapeutics, Bristol Myers Squibb, CoNCERT Pharmaceuticals (acquired by Sun Pharma in March 2023), Eli Lilly, and Pfizer; and as a speaker for Eli Lilly. **MS** has served as a speaker for Eli Lilly and Pfizer; has been a principal investigator and has received research funding from CoNCERT Pharmaceuticals (acquired by Sun Pharma in March 2023), Eli Lilly, Follica, LEO Pharma, and Santiste Medical; and has been a consultant and/or scientific/medical adviser for American Hair Research Society, Eli Lilly, Follica, Kintor, L'Oreal, National Alopecia Areata Foundation, Pfizer, and Scarring Alopecia Foundation. **AM** has been a consultant for AbbVie, Boehringer Ingelheim, CoNCERT Pharmaceuticals (acquired by Sun Pharma in March 2023), Digital Diagnostics, Eli Lilly, Equillium, Hims, LEO Pharma, and Pfizer. **CH** and **JC** are employees of Sun Pharmaceutical Industries, Inc.