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Safety Assessments in the Multinational Phase 3 THRIVE-AA1 Trial With CTP-543 (Deuruxolitinib) in Adult Patients With Moderate-to-Severe Alopecia Areata

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Background, Methods and Baseline Characteristics

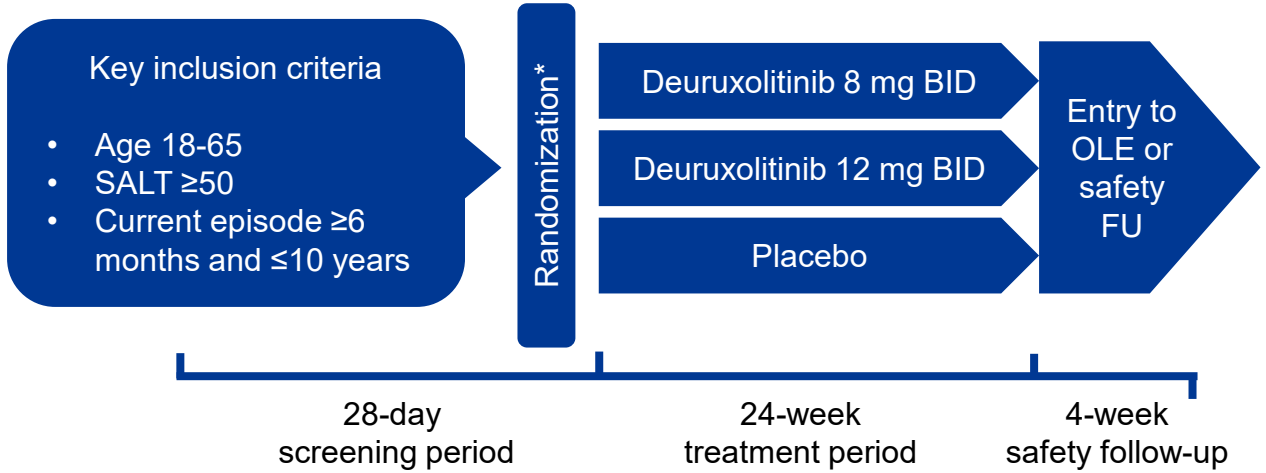
Background

- AA is an autoimmune disorder causing partial or complete loss of hair, leading to reduced quality of life and considerable psychosocial impact for patients[1]
- JAK inhibitors have been shown to reverse hair loss in AA patients[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]
- Key efficacy data from the THRIVE-AA1 study will be shown in presentations 41701, 42746 and 42752

Objective

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

THRIVE-AA1 Study Design



Key safety endpoints: TEAEs, vital signs, clinical laboratory results

Demographics/baseline 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)
Baseline total SALT score, mean (SD)	88.1 (15.10)	85.5 (18.35)	85.2 (18.41)	85.9 (17.78)

*Randomization 3:5:2 to deuruxolitinib 12 mg BID, 8 mg BID or placebo.
AA, alopecia areata; BID, twice daily; FU, follow-up; OLE, open-label extension; SALT, severity of alopecia too; SD, standard deviation; TEAE, treatment-emergent adverse event.

1. Lintzeri DA, et al. *J Dtsch Dermatol Ges.* 2022;20(1):59-90; 2. Dillon KL, et al. *Clin Cosmet Investig Dermatol.* 2021;14:691-714; 3. King B, et al. *J Am Acad Dermatol.* 2022;87(2):306-313.

Results: Key Safety Outcomes

Key safety outcomes during the 24-week study period	Placebo (n = 140)	Deuruxolitinib 8 mg BID (n = 350)	Deuruxolitinib 12 mg BID (n = 215)	Total (n = 705)
Patients with ≥1 TEAE, n (%)	78 (55.7)	228 (65.1)	137 (63.7)	443 (62.8)
Patients with serious TEAEs, n %	4 (2.9)	4 (1.1)	1 (0.5)	9 (1.3)
Related events, n	0	2	0	2
Patients with related serious TEAEs, n %	0	1 (0.3)	0	1 (0.1)
TEAEs leading to study drug discontinuation, n (%)	2 (1.4)	9 (2.6)	6 (2.8)	17 (2.4)

Potentially clinically significant laboratory abnormalities in ≥1% patients*	Placebo (n = 140)	Deuruxolitinib 8 mg BID (n = 350)	Deuruxolitinib 12 mg BID (n = 215)
Neutropenia, n (%)	1 (0.7)	6 (1.7)	6 (2.8)
Lymphopenia, n (%)	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)

- Most TEAEs were mild to moderate in severity
- Only one patient (8 mg BID) reported SAEs assessed as possibly related to treatment (pyrexia and spinal meningitis)†
  - Of note: the patient had a pain stimulator implanted and spinal injection one day prior to reporting the SAEs
- TEAEs resulting in discontinuation in >1 participant: headache and increased platelet count
- No symptomatic anemia or neutropenia-associated fevers/infections were observed

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, 8mg and 12 mg deuruxolitinib BID, respectively.

*≥1% of patients in any group. Potentially clinically significant laboratory abnormalities defined as Grade 3 or 4 based on CTCAE criteria. †Drug interrupted with an outcome of recovered/resolved.

AST, aspartate aminotransferase; BID, twice daily; CTCAE, Common Terminology Criteria for Adverse Events; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

Results: Adverse Events

TEAEs in ≥5% of patients in any group, n (%)	Placebo (n = 140)	Deuruxolitinib 8 mg BID (n = 350)	Deuruxolitinib 12 mg BID (n = 215)	Total (n = 705)
COVID-19	8 (5.7)	19 (5.4)	15 (7.0)	42 (6.0)
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)
Increase in blood creatine phosphokinase	2 (1.4)	21 (6.0)	11 (5.1)	34 (4.8)
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)

Adverse events of special interest

- Infections: 5 of 705 (0.7%) of patients experienced serious infections
  - Appendicitis (3 cases; 1 in each group, including placebo); COVID-19 (1 case); meningitis (1 case)
- Herpes zoster (2 cases; 1 in the deuruxolitinib 8 mg group, and 1 in the 12 mg BID group)*
- No thromboembolic events (DVTs/PEs); no deaths

*Neither case considered related to study drug, no dose interruptions occurred and both cases recovered/resolved.
BID, twice daily; DVT, deep vein thrombosis; PE, pulmonary embolism; TEAE, treatment-emergent adverse event.

Conclusions

- Deuruxolitinib was generally well tolerated at both the 8 mg 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 (DVT/PE) or deaths were observed
- Changes in laboratory parameters were generally consistent with those previously observed for JAK inhibitors[1] and were not associated with clinical signs and symptoms
- Long-term safety profile to be evaluated in the ongoing open-label extension trials (NCT03898479 and NCT05041803)

BID, twice daily; DVT, deep vein thrombosis; PE, pulmonary embolism; TEAE, treatment-emergent adverse event.

1. Gilhar A. *Lancet.* 2019;393(10169):318-319.