P6:CTP-543, A JAK1/JAK2 INHIBITOR, ACHIEVES PRIMARY ENDPOINT IN INTERIM ANALYSIS OF PHASE 2 TRIAL IN ALOPECIA AREATA

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Abstract

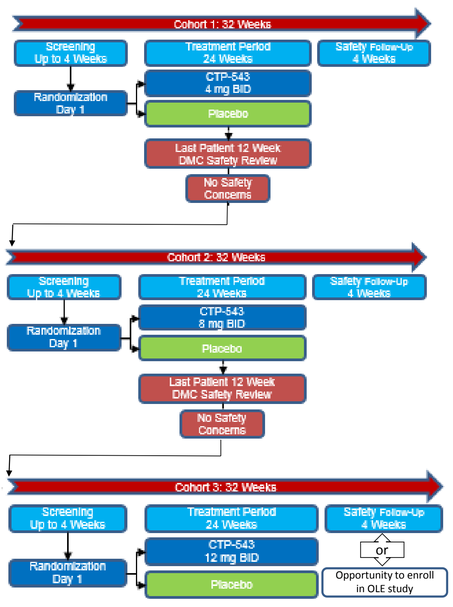
Introduction: There is growing evidence that Janus kinase (JAK) signaling contributes to the pathophysiology in alopecia areata (AA). The mechanism of hair loss in AA is believed to involve cytotoxic T cell attack of the hair follicle after loss of immune privilege, regulated by upstream JAK signaling. CTP-543 selectively inhibits JAK1 and JAK2. A Phase 2 dose-escalating trial was conducted to evaluate the efficacy and safety of CTP-543 in adults with moderate-to-severe AA. Results from the completed 4 and 8 mg BID cohorts are reported. The trial is ongoing and dosing in the final cohort, 12 mg BID, is underway.

Methods: In this randomized, double-blind, placebo-controlled Phase 2 trial, adult AA patients (18-65 years) having at least 50% hair loss were sequentially randomized to receive CTP-543 or placebo BID for 24 weeks. For this interim analysis subjects received either placebo, 4, or 8 mg BID. Hair loss was measured by Severity of Alopecia Tool (SALT). The primary endpoint was the percentage of patients achieving at least a 50% relative reduction in SALT between Week 24 and baseline. Safety was assessed by adverse event reporting, physical examination, and clinical laboratory assessments.

Results: For this analysis, a total of 104 patients were randomly assigned to receive either 4 mg BID CTP-543 (N = 30), 8 mg BID CTP-543 (N = 38) or placebo BID (N = 36). At Week 24, 47% of patients treated with 8 mg BID of CTP-543 achieved a ≥ 50% reduction in their overall SALT score compared to 8.6% for placebo ($p < 0.001$). 21% of patients treated with 4 mg BID of CTP-543 achieved a ≥ 50% reduction in their overall SALT score compared to 8.6% for placebo (NS). The 8 mg BID dose group was significantly different from the 4 mg BID dose group ($p < 0.05$). The percentage of patients achieving the primary endpoint continued to increase at Week 24. The most commonly reported adverse events were headache, upper respiratory tract infection, cough, acne and nausea. No significant laboratory abnormalities were noted. No serious adverse events were reported.

Conclusions: Treatment with 8 mg BID of CTP-543 for 24 weeks resulted in significant hair regrowth in patients with AA, with an acceptable safety profile.

Sequential Trial Design



Key Entry Criteria

- At least 50% hair loss at baseline
- Current episode of hair loss > 6 months and < 10 years
- No active scalp inflammation, psoriasis, seborrheic dermatitis, scalp trauma or untreated actinic keratosis
- No current systemic immunosuppressant meds

For Further Information

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CTP-543 ClinicalTrials.gov Identifier:
- NCT03137381
- NCT03811912

Results

Trial Design:

- Double-blind, randomized, placebo-controlled trial in adult patients with moderate-to-severe alopecia areata
- Patients sequentially randomized to receive one of three doses of CTP-543 (4, 8 and 12 mg BID) or placebo for 24 weeks
- 4 mg BID and 8 mg BID cohorts completed; 12 mg BID cohort is currently ongoing
- Primary Endpoint: 50% relative reduction in SALT between Week 24 and baseline

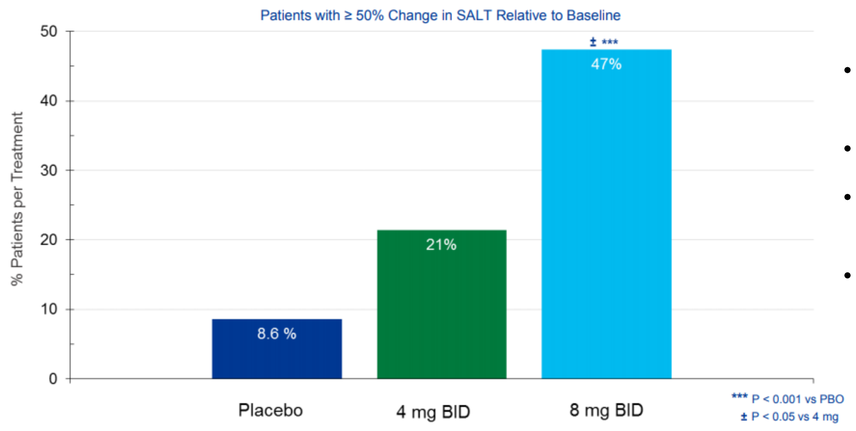
Key Demographics and Baseline Alopecia Areata Characteristics:

	Placebo	CTP-543 4 mg BID	CTP-543 8 mg BID
Efficacy Population (N)	35	28	38
Age: Yrs	37	36	37
Females, N (%)	24 (67%)	22 (73%)	26 (68%)
Episode Duration: Yrs	3.6	6	3.8
SALT score, Mean (SD)	85.0 (19.4)	88.8 (16.2)	89.1 (16.4)
AA Patchy, N(%)	19 (52.8%)	16 (53.3%)	16 (42.1%)
AA Totalis, N(%)	5 (13.9%)	2 (6.7%)	6 (15.8%)
AA Universalis, N(%)	12 (33.3%)	12 (40.0%)	14 (36.8%)
AA Ophiasis, N(%)	0 (0%)	0 (0%)	2 (5.3%)

Most Common Treatment Emergent Adverse Events by Patient:

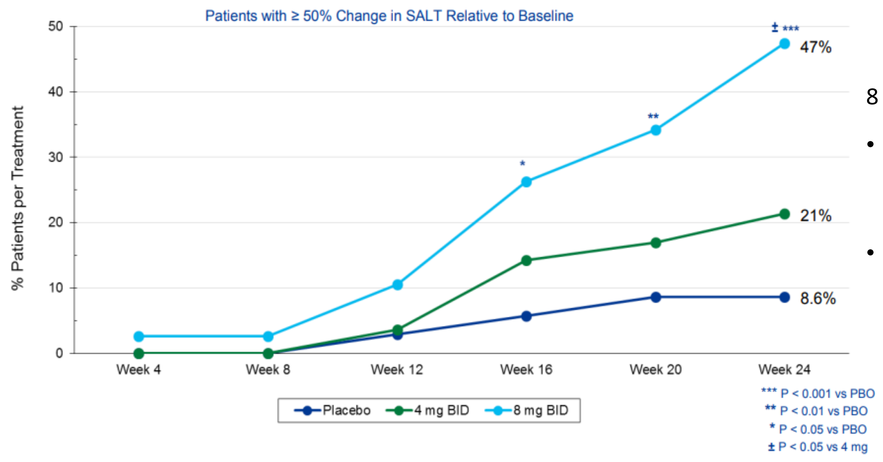
Preferred Term	Placebo	CTP-543 4 mg BID	CTP-543 8 mg BID
Headache	4 (11.1%)	5 (17.2%)	10 (26.3%)
Nausea	4 (11.1%)	4 (13.8%)	4 (10.5%)
Acne	2 (5.6%)	4 (13.8%)	4 (10.5%)
Cough	0	4 (13.8%)	1 (2.6%)
Diarrhoea	3 (8.3%)	3 (10.3%)	1 (2.6%)
Nasopharyngitis	1 (2.8%)	3 (10.3%)	3 (7.9%)
Folliculitis	0	3 (10.3%)	2 (5.3%)
Blood creatine phosphokinase increased	1 (2.8%)	3 (10.3%)	2 (5.3%)
Oropharyngeal pain	0	3 (10.3%)	1 (2.6%)
Upper respiratory tract infection	6 (16.7%)	2 (6.9%)	2 (5.3%)
Discontinuations Due to AE	3 (37.5%)	0 (0%)	2 (25%)

Primary Analysis: Responders at Week 24



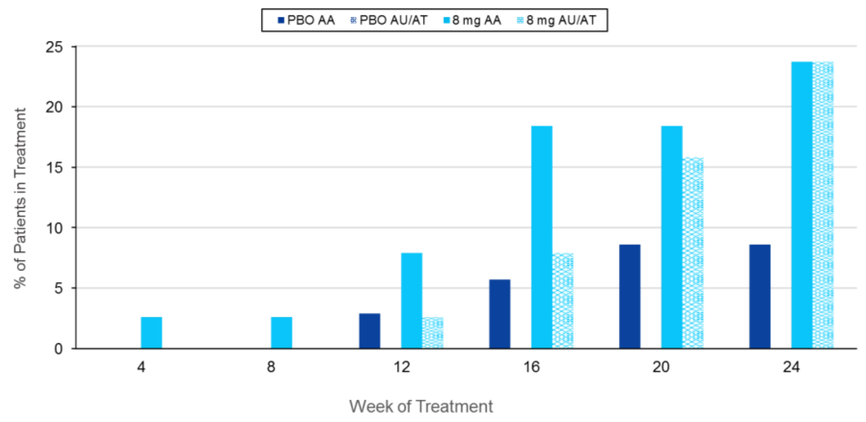
- Primary Endpoint met with 8 mg BID dose ($p < 0.001$ vs PBO)
- 4 mg BID NS ($p > 0.05$)
- 8 mg BID significantly different from 4 mg BID ($p < 0.05$)
- Clear dose response relationship – 8 mg BID is Minimum Effective Dose

Responders by Visit



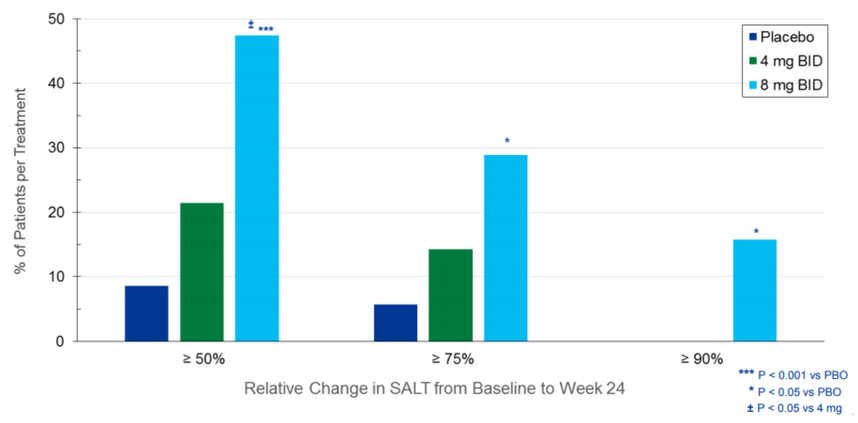
8 mg BID:
- Steady improvement in SALT responders starting at Week 8
- No plateauing of response rate at Week 24

Responder by Alopecia Areata Subtype



- Equal responder rate for patients with complete scalp hair loss vs. patchy loss by Week 24
- No "ceiling effect"
- 8 mg BID responder as early as Week 4
- PBO responders all had patchy AA

Patient SALT Improvement

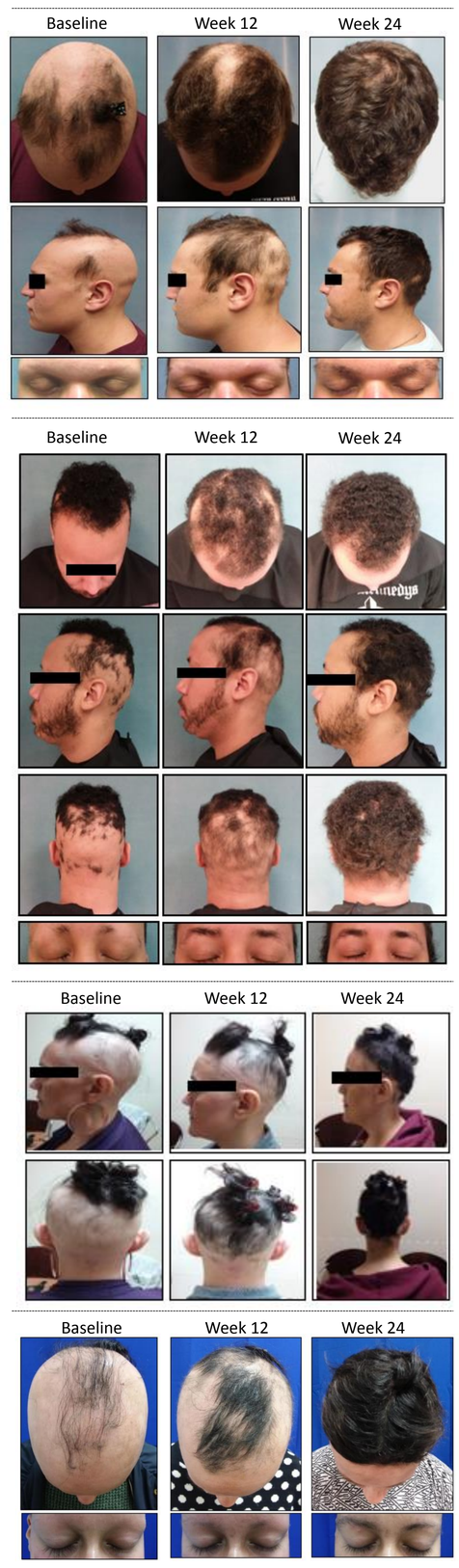


8 mg BID:
- Results in significant hair regrowth
- 29% achieving ≥ 75% relative SALT change
- 16% achieving ≥ 90% relative SALT change

Conclusions

Phase 2 interim analysis showed:

- 4 mg BID and 8 mg BID CTP-543 generally well-tolerated
  - The most common side effects were headache, upper respiratory tract infection, cough, acne and nausea
  - No serious adverse events were reported
- Primary endpoint met with 8 mg BID
  - 8 mg BID dose group was significantly different from placebo and 4 mg BID dose groups
  - 8 mg BID determined to be the minimally effective dose
  - Response did not appear to have plateaued at Week 24
- Significant changes in SALT score were observed starting at 12 weeks
- Similar overall scalp regrowth response rate between patchy AA and AU/AT



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