



## Clinical trial results:

### A Double-Blind, Randomized, Placebo-Controlled Study to Evaluate the Efficacy and Safety of CTP-543 in Adult Subjects with Moderate to Severe Alopecia Areata (THRIVE-AA1)

#### Summary

EudraCT number	2020-002704-40
Trial protocol	FR
Global end of trial date	19 April 2022

#### Results information

Result version number	v1 (current)
This version publication date	23 April 2023
First version publication date	23 April 2023

#### Trial information

##### Trial identification

Sponsor protocol code	CP543.3001
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04518995
WHO universal trial number (UTN)	-

Notes:

#### Sponsors

Sponsor organisation name	Concert Pharmaceuticals, Inc.
Sponsor organisation address	65 Hayden Avenue, Lexington, MA, United States, 02421
Public contact	Medical Manager, Linical France SARL, +40 256207271, diana.chera@linical.com
Scientific contact	Medical Manager, Linical France SARL, +40 256207271, diana.chera@linical.com

Notes:

#### Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

## Results analysis stage

Analysis stage	Final
Date of interim/final analysis	19 April 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	19 April 2022
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

The primary purpose of this study was to assess the safety and efficacy of CTP-543 on regrowth of hair following 24 weeks of treatment.

Protection of trial subjects:

All study subjects were required to read and sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 November 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 50
Country: Number of subjects enrolled	Spain: 19
Country: Number of subjects enrolled	France: 50
Country: Number of subjects enrolled	United States: 375
Country: Number of subjects enrolled	Canada: 212
Worldwide total number of subjects	706
EEA total number of subjects	119

Notes:

### Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	703
From 65 to 84 years	3

85 years and over	0
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## Subject disposition

### Recruitment

Recruitment details:

Subjects were enrolled at study centers in Canada, France, Poland, Spain, and the United States from 23 November 2020 to 19 April 2022.

### Pre-assignment

Screening details:

946 subjects were screened, out of which 706 subjects who experienced moderate to severe hair loss due to alopecia areata were enrolled to receive CTP-543 or placebo.

### Period 1

Period 1 title	Overall study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Placebo

Arm description:

Subjects received CTP-543 matched placebo tablets, orally, twice daily (BID) for up to 24 weeks.

Arm type	Placebo
Investigational medicinal product name	CTP-543 matching placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

CTP-543 matched placebo administered BID for up to 24 weeks.

<b>Arm title</b>	CTP-543 8 mg BID
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Arm description:

Subjects received CTP-543 8 mg tablets, orally, BID for up to 24 weeks.

Arm type	Experimental
Investigational medicinal product name	CTP-543
Investigational medicinal product code	
Other name	Deuruxolitinib
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

CTP-543 administered BID for up to 24 weeks.

<b>Arm title</b>	CTP-543 12 mg BID
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Arm description:

Subjects received CTP-543 12 mg tablets, orally, BID for up to 24 weeks.

Arm type	Experimental
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Investigational medicinal product name	CTP-543
Investigational medicinal product code	
Other name	Deuruxolitinib
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

CTP-543 administered BID for up to 24 weeks.

<b>Number of subjects in period 1</b>	Placebo	CTP-543 8 mg BID	CTP-543 12 mg BID
Started	140	351	215
Completed	129	318	199
Not completed	11	33	16
Non-compliance with Study Drug	-	3	2
Protocol violation	2	-	1
Pregnancy	-	-	1
Reason not specified	4	11	2
Lost to follow-up	1	10	6
Treatment Emergent or Worsening Adverse Event	2	8	4
Lack of efficacy	2	1	-

## Baseline characteristics

### Reporting groups

Reporting group title	Placebo
Reporting group description:	
Subjects received CTP-543 matched placebo tablets, orally, twice daily (BID) for up to 24 weeks.	
Reporting group title	CTP-543 8 mg BID
Reporting group description:	
Subjects received CTP-543 8 mg tablets, orally, BID for up to 24 weeks.	
Reporting group title	CTP-543 12 mg BID
Reporting group description:	
Subjects received CTP-543 12 mg tablets, orally, BID for up to 24 weeks.	

Reporting group values	Placebo	CTP-543 8 mg BID	CTP-543 12 mg BID
Number of subjects	140	351	215
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean	38.7	38.9	38.2
standard deviation	± 13.81	± 13.32	± 12.80
Gender categorical			
Units: Subjects			
Female	89	217	131
Male	51	134	84
Ethnicity			
Units: Subjects			
Hispanic or Latino	11	30	13
Not Hispanic or Latino	119	292	188
Unknown	10	29	14
Race			
Units: Subjects			
American Indian or Alaska Native	0	2	1
Asian	10	22	21
Black or African American	16	40	27
Native Hawaiian or other Pacific Islander	1	3	1
White	98	241	145
Other	5	17	6
Not reported	10	26	14

Reporting group values	Total		
Number of subjects	706		
Age categorical			
Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	-		
Gender categorical Units: Subjects			
Female	437		
Male	269		
Ethnicity Units: Subjects			
Hispanic or Latino	54		
Not Hispanic or Latino	599		
Unknown	53		
Race Units: Subjects			
American Indian or Alaska Native	3		
Asian	53		
Black or African American	83		
Native Hawaiian or other Pacific Islander	5		
White	484		
Other	28		
Not reported	50		

## End points

### End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Subjects received CTP-543 matched placebo tablets, orally, twice daily (BID) for up to 24 weeks.	
Reporting group title	CTP-543 8 mg BID
Reporting group description:	
Subjects received CTP-543 8 mg tablets, orally, BID for up to 24 weeks.	
Reporting group title	CTP-543 12 mg BID
Reporting group description:	
Subjects received CTP-543 12 mg tablets, orally, BID for up to 24 weeks.	

### Primary: Percentage of Subjects Achieving an Absolute Severity of Alopecia Tool (SALT) Score of $\leq 20$ at Week 24

End point title	Percentage of Subjects Achieving an Absolute Severity of Alopecia Tool (SALT) Score of $\leq 20$ at Week 24
End point description:	
SALT is a quantitative assessment of scalp hair loss with scores ranging in severity from 0 (no scalp hair loss) to a maximum of 100 (complete scalp hair loss). Efficacy population included all subjects who were randomised in the study and dispensed study drug during the treatment period.	
End point type	Primary
End point timeframe:	
Week 24	

End point values	Placebo	CTP-543 8 mg BID	CTP-543 12 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	140	351	215	
Units: percentage of subjects				
number (not applicable)	0.8	29.6	41.5	

### Statistical analyses

Statistical analysis title	Placebo vs CTP-543 8 mg BID
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	491
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[1]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.28



Confidence interval	
level	95 %
sides	2-sided
lower limit	0.23
upper limit	0.33
Variability estimate	Standard error of the mean
Dispersion value	0.026

Notes:

[1] - P-value was calculated by Mantel-Haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	355
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[2]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.32
upper limit	0.46
Variability estimate	Standard error of the mean
Dispersion value	0.034

Notes:

[2] - P-value was calculated by Mantel-Haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

### **Secondary: Percentage of Responders on the Hair Satisfaction Patient Reported Outcome (SPRO) Scale at Weeks 12, 16, 20, and 24**

End point title	Percentage of Responders on the Hair Satisfaction Patient Reported Outcome (SPRO) Scale at Weeks 12, 16, 20, and 24
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End point description:

SPRO is a questionnaire answered by the subject and designed to measure how satisfied alopecia areata subjects are with their hair at the time of the assessment. The responses range from 1 to 5: 1= very satisfied, 2= satisfied, 3= neither satisfied nor dissatisfied, 4= dissatisfied, and 5= very dissatisfied. Responders were defined as subjects with responses of "satisfied" or "very satisfied". Efficacy population included all subjects who were randomised in the study and dispensed study drug during the treatment period.

End point type	Secondary
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End point timeframe:

Weeks 12, 16, 20, and 24

End point values	Placebo	CTP-543 8 mg BID	CTP-543 12 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	140	351	215	
Units: percentage of responders				
number (not applicable)				
Week 12	11.9	35.3	46.4	
Week 16	8.3	38.2	51.5	
Week 20	6.1	37.4	54.0	
Week 24	4.7	42.1	53.0	

## Statistical analyses

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description: Week 12	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	491
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[3]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.17
upper limit	0.32
Variability estimate	Standard error of the mean
Dispersion value	0.038

Notes:

[3] - P-value was calculated by Mantel-Haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description: Week 12	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	355
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[4]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.35

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.26
upper limit	0.43
Variability estimate	Standard error of the mean
Dispersion value	0.044

Notes:

[4] - P-value was calculated by Mantel-Haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
Week 16	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	491
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[5]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.24
upper limit	0.38
Variability estimate	Standard error of the mean
Dispersion value	0.035

Notes:

[5] - P-value was calculated by Mantel-Haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
Week 16	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	355
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[6]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.35
upper limit	0.51
Variability estimate	Standard error of the mean
Dispersion value	0.041

Notes:

[6] - P-value was calculated by Mantel-Haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
Week 20	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	491
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[7]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.26
upper limit	0.39
Variability estimate	Standard error of the mean
Dispersion value	0.033

Notes:

[7] - P-value was calculated by Mantel-Haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
Week 20	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	355
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[8]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.39
upper limit	0.55
Variability estimate	Standard error of the mean
Dispersion value	0.04

Notes:

[8] - P-value was calculated by Mantel-Haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
Week 24	
Comparison groups	Placebo v CTP-543 8 mg BID

Number of subjects included in analysis	491
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[9]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.31
upper limit	0.44
Variability estimate	Standard error of the mean
Dispersion value	0.033

Notes:

[9] - P-value was calculated by Mantel-Haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
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Statistical analysis description:

Week 24

Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	355
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[10]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.39
upper limit	0.55
Variability estimate	Standard error of the mean
Dispersion value	0.039

Notes:

[10] - P-value was calculated by Mantel-Haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

### **Secondary: Percentage of Subjects Achieving an Absolute SALT Score of ≤20 at Weeks 4, 8, 12, 16, and 20**

End point title	Percentage of Subjects Achieving an Absolute SALT Score of ≤20 at Weeks 4, 8, 12, 16, and 20
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End point description:

SALT is a quantitative assessment of scalp hair loss with scores ranging in severity from 0 (no scalp hair loss) to a maximum of 100 (complete scalp hair loss). Efficacy population included all subjects who were randomised in the study and dispensed study drug during the treatment period.

End point type	Secondary
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End point timeframe:

Weeks 4, 8, 12, 16, and 20

<b>End point values</b>	Placebo	CTP-543 8 mg BID	CTP-543 12 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	140	351	215	
Units: percentage of subjects				
number (not applicable)				
Week 4	0	0.9	0	
Week 8	0	3.3	6.1	
Week 12	0.7	10.4	18.2	
Week 16	2.3	16.5	29.6	
Week 20	0.8	24.1	37.0	

## Statistical analyses

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
Week 4	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	491
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0816 <sup>[11]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0.02
Variability estimate	Standard error of the mean
Dispersion value	0.005

Notes:

[11] - P-value was calculated by Mantel-Haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
Week 8	
Comparison groups	Placebo v CTP-543 8 mg BID

Number of subjects included in analysis	491
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0005 <sup>[12]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.01
upper limit	0.05
Variability estimate	Standard error of the mean
Dispersion value	0.01

Notes:

[12] - P-value was calculated by Mantel-Haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
Week 8	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	355
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0002 <sup>[13]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.03
upper limit	0.09
Variability estimate	Standard error of the mean
Dispersion value	0.016

Notes:

[13] - P-value was calculated by Mantel-Haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
Week 12	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	491
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[14]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.1

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.06
upper limit	0.14
Variability estimate	Standard error of the mean
Dispersion value	0.018

Notes:

[14] - P-value was calculated by Mantel-Haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
Week 12	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	355
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[15]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.12
upper limit	0.22
Variability estimate	Standard error of the mean
Dispersion value	0.027

Notes:

[15] - P-value was calculated by Mantel-Haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
Week 16	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	491
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[16]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.1
upper limit	0.19
Variability estimate	Standard error of the mean
Dispersion value	0.024



Notes:

[16] - P-value was calculated by Mantel-Haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
Week 16	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	355
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[17]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.2
upper limit	0.33
Variability estimate	Standard error of the mean
Dispersion value	0.033

Notes:

[17] - P-value was calculated by Mantel-Haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
Week 20	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	491
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[18]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.19
upper limit	0.28
Variability estimate	Standard error of the mean
Dispersion value	0.024

Notes:

[18] - P-value was calculated by Mantel-Haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
Week 20	
Comparison groups	Placebo v CTP-543 12 mg BID

Number of subjects included in analysis	355
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[19]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.28
upper limit	0.41
Variability estimate	Standard error of the mean
Dispersion value	0.034

Notes:

[19] - P-value was calculated by Mantel-Haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

### Secondary: Relative Change in SALT Scores From Baseline at Weeks 4, 8, 12, 16, 20, and 24

End point title	Relative Change in SALT Scores From Baseline at Weeks 4, 8, 12, 16, 20, and 24
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End point description:

SALT is a quantitative assessment of scalp hair loss with scores ranging in severity from 0 (no scalp hair loss) to a maximum of 100 (complete scalp hair loss). Relative change (percent change) to baseline (CFB) is calculated as:  $100 \times ([\text{post-baseline SALT score} - \text{baseline SALT score}] / \text{baseline SALT score})$ . Efficacy population included all subjects who were randomised in the study and dispensed study drug during the treatment period. Overall number of subjects analysed indicates the number of subjects with data available for analysis of this end point. Number of subjects analysed indicates the number of subjects with data available for analysis at the specified timepoint.

End point type	Secondary
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End point timeframe:

Baseline, Weeks 4, 8, 12, 16, 20, and 24

End point values	Placebo	CTP-543 8 mg BID	CTP-543 12 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	139	345	212	
Units: percent change				
arithmetic mean (standard deviation)				
Relative CFB at Week 4 (n= 139, 345, 211)	-0.2 (± 5.59)	-2.6 (± 12.79)	-4.0 (± 12.03)	
Relative CFB at Week 8 (n= 138, 336, 212)	-2.3 (± 11.41)	-10.9 (± 21.00)	-17.5 (± 27.16)	
Relative CFB at Week 12 (n= 136, 328, 209)	-0.6 (± 16.63)	-22.2 (± 29.45)	-31.1 (± 35.53)	
Relative CFB at Week 16 (n= 131, 322, 203)	-1.8 (± 21.06)	-30.3 (± 34.20)	-41.2 (± 38.95)	
Relative CFB at Week 20 (n= 131, 316, 200)	-1.3 (± 22.14)	-36.0 (± 37.82)	-46.8 (± 41.32)	
Relative CFB at Week 24 (n= 128, 318, 200)	-1.5 (± 23.30)	-41.2 (± 39.37)	-50.4 (± 41.52)	

## Statistical analyses

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description: Week 4	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	484
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0564 <sup>[20]</sup>
Method	MMRM
Parameter estimate	Least Square (LS) Mean Difference
Point estimate	-2.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.4
upper limit	0.1
Variability estimate	Standard error of the mean
Dispersion value	1.13

Notes:

[20] - P-value was calculated by mixed model repeated measures (MMRM) analysis with effects for treatment, visit, treatment-by-visit interaction, and baseline value.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description: Week 4	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	351
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0054 <sup>[21]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-3.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.9
upper limit	-1
Variability estimate	Standard error of the mean
Dispersion value	1.23

Notes:

[21] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, and baseline value.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
Week 8	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	484
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[22]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-8.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.7
upper limit	-4.3
Variability estimate	Standard error of the mean
Dispersion value	2.16

Notes:

[22] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, and baseline value.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
Week 8	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	351
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[23]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-14.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-19.5
upper limit	-10.3
Variability estimate	Standard error of the mean
Dispersion value	2.34

Notes:

[23] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, and baseline value.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
Week 12	
Comparison groups	Placebo v CTP-543 8 mg BID

Number of subjects included in analysis	484
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[24]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-21.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-27.5
upper limit	-16
Variability estimate	Standard error of the mean
Dispersion value	2.94

Notes:

[24] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, and baseline value.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
Week 12	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	351
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[25]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-30
Confidence interval	
level	95 %
sides	2-sided
lower limit	-36.3
upper limit	-23.8
Variability estimate	Standard error of the mean
Dispersion value	3.19

Notes:

[25] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, and baseline value.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
Week 16	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	484
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[26]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-28.4

Confidence interval	
level	95 %
sides	2-sided
lower limit	-35.1
upper limit	-21.8
Variability estimate	Standard error of the mean
Dispersion value	3.38

Notes:

[26] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, and baseline value.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
Week 16	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	351
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [27]
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-38.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-45.7
upper limit	-31.3
Variability estimate	Standard error of the mean
Dispersion value	3.66

Notes:

[27] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, and baseline value.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
Week 20	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	484
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [28]
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-34.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-42.1
upper limit	-27.7
Variability estimate	Standard error of the mean
Dispersion value	3.66

Notes:

[28] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, and baseline value.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
Week 20	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	351
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [29]
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-44.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-52.3
upper limit	-36.8
Variability estimate	Standard error of the mean
Dispersion value	3.96

Notes:

[29] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, and baseline value.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
Week 24	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	484
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [30]
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-39.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-46.7
upper limit	-31.8
Variability estimate	Standard error of the mean
Dispersion value	3.79

Notes:

[30] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, and baseline value.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
Week 24	
Comparison groups	Placebo v CTP-543 12 mg BID

Number of subjects included in analysis	351
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[31]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-47
Confidence interval	
level	95 %
sides	2-sided
lower limit	-55.1
upper limit	-39
Variability estimate	Standard error of the mean
Dispersion value	4.1

Notes:

[31] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, and baseline value.

### Secondary: Percentage of Responders Assessed Using the Clinician Global Impression of Improvement (CGI-I) at Weeks 12, 16, 20, and 24

End point title	Percentage of Responders Assessed Using the Clinician Global Impression of Improvement (CGI-I) at Weeks 12, 16, 20, and 24
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End point description:

The CGI-I is a questionnaire that asks the clinician to evaluate the improvement or worsening of the subject's alopecia areata as compared to the start of the study on a 7-point scale. Responses range from 1 (very much worse) to 7 (very much improved). Responders were defined as subjects with responses of 6 (much improved) or 7 (very much improved). Efficacy population included all subjects who were randomised in the study and dispensed study drug during the treatment period.

End point type	Secondary
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End point timeframe:

Weeks 12, 16, 20, and 24

End point values	Placebo	CTP-543 8 mg BID	CTP-543 12 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	140	351	215	
Units: percentage of responders				
number (not applicable)				
Weeks 12	3.7	36.3	43.5	
Weeks 16	7.7	44.2	54.7	
Weeks 20	8.4	49.1	57.1	
Weeks 24	9.4	53.8	59.8	

### Statistical analyses

Statistical analysis title	Placebo vs CTP-543 8 mg BID
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Statistical analysis description:

Week 12



Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	491
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[32]</sup>
Method	Cochran-Mantel-Haenszel

Notes:

[32] - P-value was calculated by cochrane mantel haenszel (CMH) test stratified by baseline scalp hair loss (partial vs complete/near-complete) for responders in each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
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Statistical analysis description:

Week 12

Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	355
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[33]</sup>
Method	Cochran-Mantel-Haenszel

Notes:

[33] - P-value was calculated by CMH test stratified by baseline scalp hair loss (partial vs complete/near-complete) for responders in each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
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Statistical analysis description:

Week 16

Comparison groups	CTP-543 8 mg BID v Placebo
Number of subjects included in analysis	491
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[34]</sup>
Method	Cochran-Mantel-Haenszel

Notes:

[34] - P-value was calculated by CMH test stratified by baseline scalp hair loss (partial vs complete/near-complete) for responders in each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
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Statistical analysis description:

Week 16

Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	355
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[35]</sup>
Method	Cochran-Mantel-Haenszel

Notes:

[35] - P-value was calculated by CMH test stratified by baseline scalp hair loss (partial vs complete/near-complete) for responders in each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
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Statistical analysis description:

Week 20

Comparison groups	Placebo v CTP-543 8 mg BID
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Number of subjects included in analysis	491
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[36]</sup>
Method	Cochran-Mantel-Haenszel

Notes:

[36] - P-value was calculated by CMH test stratified by baseline scalp hair loss (partial vs complete/near-complete) for responders in each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
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Statistical analysis description:

Week 20

Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	355
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[37]</sup>
Method	Cochran-Mantel-Haenszel

Notes:

[37] - P-value was calculated by CMH test stratified by baseline scalp hair loss (partial vs complete/near-complete) for responders in each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
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Statistical analysis description:

Week 24

Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	491
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[38]</sup>
Method	Cochran-Mantel-Haenszel

Notes:

[38] - P-value was calculated by CMH test stratified by baseline scalp hair loss (partial vs complete/near-complete) for responders in each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
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Statistical analysis description:

Week 24

Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	355
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[39]</sup>
Method	Cochran-Mantel-Haenszel

Notes:

[39] - P-value was calculated by CMH test stratified by baseline scalp hair loss (partial vs complete/near-complete) for responders in each treatment group compared to placebo.

## **Secondary: Percentage of Responders Assessed Using the Patient Global Impression of Improvement (PGI-I) at Weeks 12, 16, 20, and 24**

End point title	Percentage of Responders Assessed Using the Patient Global Impression of Improvement (PGI-I) at Weeks 12, 16, 20, and 24
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**End point description:**

The PGI-I is a self-administered questionnaire that asks the subject to evaluate the improvement or worsening of their alopecia areata as compared to the start of the study on a 7-point scale. Responses range from 1 (very much worse) to 7 (very much improved). Responders were defined as subjects with responses of 6 (much improved) or 7 (very much improved). Efficacy population included all subjects who were randomised in the study and dispensed study drug during the treatment period.

End point type	Secondary
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**End point timeframe:**

Weeks 12, 16, 20, and 24

End point values	Placebo	CTP-543 8 mg BID	CTP-543 12 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	140	351	215	
Units: percentage of responders				
number (not applicable)				
Week 12	6.7	38.9	49.8	
Week 16	9.0	49.1	58.3	
Week 20	10.0	50.6	60.0	
Week 24	10.2	56.6	65.5	

**Statistical analyses**

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
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**Statistical analysis description:**

Week 12

Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	491
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[40]</sup>
Method	Cochran-Mantel-Haenszel

**Notes:**

[40] - P-value was calculated by CMH test stratified by baseline scalp hair loss (partial vs complete/near-complete) for responders in each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
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**Statistical analysis description:**

Week 12

Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	355
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[41]</sup>
Method	Cochran-Mantel-Haenszel

**Notes:**

[41] - P-value was calculated by CMH test stratified by baseline scalp hair loss (partial vs complete/near-complete) for responders in each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
Week 16	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	491
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[42]</sup>
Method	Cochran-Mantel-Haenszel

Notes:

[42] - P-value was calculated by CMH test stratified by baseline scalp hair loss (partial vs complete/near-complete) for responders in each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
Week 16	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	355
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[43]</sup>
Method	Cochran-Mantel-Haenszel

Notes:

[43] - P-value was calculated by CMH test stratified by baseline scalp hair loss (partial vs complete/near-complete) for responders in each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
Week 20	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	491
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[44]</sup>
Method	Cochran-Mantel-Haenszel

Notes:

[44] - P-value was calculated by CMH test stratified by baseline scalp hair loss (partial vs complete/near-complete) for responders in each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
Week 20	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	355
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[45]</sup>
Method	Cochran-Mantel-Haenszel

Notes:

[45] - P-value was calculated by CMH test stratified by baseline scalp hair loss (partial vs complete/near-complete) for responders in each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
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## Statistical analysis description:

Week 24

Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	491
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [46]
Method	Cochran-Mantel-Haenszel

Notes:

[46] - P-value was calculated by CMH test stratified by baseline scalp hair loss (partial vs complete/near-complete) for responders in each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
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## Statistical analysis description:

Week 24

Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	355
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [47]
Method	Cochran-Mantel-Haenszel

Notes:

[47] - P-value was calculated by CMH test stratified by baseline scalp hair loss (partial vs complete/near-complete) for responders in each treatment group compared to placebo.

## Secondary: Change in the Clinician Global Impression of Severity (CGI-S) Scores From Baseline at Weeks 12, 16, 20, and 24

End point title	Change in the Clinician Global Impression of Severity (CGI-S) Scores From Baseline at Weeks 12, 16, 20, and 24
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End point description:

The CGI-S is a questionnaire that asks the clinician to evaluate the symptom severity of the subject's alopecia areata at the time of assessment. The symptom severity was rated on a scale ranging from 1 to 7, where 1=normal, no hair loss; 2=borderline hair loss; 3=mild hair loss; 4=moderate hair loss; 5=marked hair loss; 6=severe hair loss; 7=among the most extreme hair loss. Higher scores indicate more hair loss. A negative change from baseline indicates (CFB) less hair loss. Efficacy population included all subjects who were randomised in the study and dispensed study drug during the treatment period. Overall number of subjects analysed indicates the number of subjects with data available for analysis of this end point. Number of subjects analysed indicates the number of subjects with data available for analysis at the specified timepoint.

End point type	Secondary
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End point timeframe:

Baseline, Weeks 12, 16, 20, and 24

End point values	Placebo	CTP-543 8 mg BID	CTP-543 12 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	136	328	209	
Units: score on a scale				
arithmetic mean (standard deviation)				
Baseline	6.5 (± 0.74)	6.4 (± 0.86)	6.4 (± 0.76)	
CFB at Week 12 (n= 136, 327, 209)	-0.1 (± 0.74)	-1.0 (± 1.38)	-1.4 (± 1.53)	
CFB at Week 16 (n= 131, 321, 203)	-0.2 (± 0.99)	-1.3 (± 1.55)	-1.9 (± 1.77)	
CFB at Week 20 (n= 131, 314, 200)	-0.1 (± 0.83)	-1.6 (± 1.77)	-2.2 (± 1.92)	

CFB at Week 24 (n= 127, 317, 200)	-0.2 ( $\pm$ 0.90)	-1.9 ( $\pm$ 1.89)	-2.4 ( $\pm$ 2.03)	
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## Statistical analyses

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description: Week 12	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	464
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[48]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	-0.7
Variability estimate	Standard error of the mean
Dispersion value	0.13

Notes:

[48] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description: Week 12	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	345
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[49]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	-0.9
Variability estimate	Standard error of the mean
Dispersion value	0.14

Notes:

[49] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
Week 16	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	464
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[50]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	-0.9
Variability estimate	Standard error of the mean
Dispersion value	0.15

Notes:

[50] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
Week 16	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	345
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[51]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.9
upper limit	-1.3
Variability estimate	Standard error of the mean
Dispersion value	0.16

Notes:

[51] - CFB in the CGI-S score was analysed using mixed model repeated measures analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
Week 20	
Comparison groups	Placebo v CTP-543 8 mg BID

Number of subjects included in analysis	464
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[52]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.8
upper limit	-1.2
Variability estimate	Standard error of the mean
Dispersion value	0.16

Notes:

[52] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
Week 20	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	345
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[53]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.3
upper limit	-1.6
Variability estimate	Standard error of the mean
Dispersion value	0.18

Notes:

[53] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
Week 24	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	464
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[54]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.7



Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	-1.3
Variability estimate	Standard error of the mean
Dispersion value	0.18

Notes:

[54] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
Week 24	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	345
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [55]
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-2.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.5
upper limit	-1.7
Variability estimate	Standard error of the mean
Dispersion value	0.19

Notes:

[55] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

### **Secondary: Change in the Patient Global Impression of Severity (PGI-S) Scores From Baseline at Weeks 12, 16, 20, and 24**

End point title	Change in the Patient Global Impression of Severity (PGI-S) Scores From Baseline at Weeks 12, 16, 20, and 24
End point description:	
<p>The PGI-S is a self-administered questionnaire that asks the subject to evaluate the symptom severity of their alopecia areata at the time of assessment. Symptom severity was rated on a scale ranging from 1 to 7, where 1= normal, no hair loss; 2= borderline hair loss; 3= mild hair loss; 4= moderate hair loss; 5= marked hair loss; 6= severe hair loss; 7= among the most extreme hair loss. Higher scores indicate more hair loss. A negative CFB indicates less hair loss. Efficacy population included all subjects who were randomised in the study and dispensed study drug during the treatment period. Overall number of subjects analysed indicates the number of subjects with data available for analysis of this end point. Number of subjects analysed indicates the number of subjects with data available for analysis at the specified timepoint.</p>	
End point type	Secondary
End point timeframe:	
Baseline, Weeks 12, 16, 20, and 24	

End point values	Placebo	CTP-543 8 mg BID	CTP-543 12 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	137	329	209	
Units: score on a scale				
arithmetic mean (standard deviation)				
Baseline	6.5 (± 0.76)	6.5 (± 0.80)	6.4 (± 0.86)	
CFB at Week 12 (n= 135, 329, 209)	-0.4 (± 1.08)	-1.1 (± 1.64)	-1.4 (± 1.79)	
CFB at Week 16 (n= 133, 322, 204)	-0.2 (± 0.78)	-1.5 (± 1.83)	-2.0 (± 1.95)	
CFB at Week 20 (n= 130, 318, 200)	-0.3 (± 1.01)	-1.8 (± 2.01)	-2.2 (± 2.07)	
CFB at Week 24 (n= 128, 318, 200)	-0.1 (± 0.74)	-1.9 (± 2.05)	-2.4 (± 2.14)	

## Statistical analyses

Statistical analysis title	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
Week 12	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	466
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[56]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	-0.3
Variability estimate	Standard error of the mean
Dispersion value	0.16

Notes:

[56] - P-value was calculated by MMRM with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

Statistical analysis title	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
Week 12	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	346
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[57]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	-0.6
Variability estimate	Standard error of the mean
Dispersion value	0.17

Notes:

[57] - P-value was calculated by MMRM with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
Week 16	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	466
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[58]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.6
upper limit	-0.9
Variability estimate	Standard error of the mean
Dispersion value	0.17

Notes:

[58] - P-value was calculated by MMRM with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
Week 16	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	346
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[59]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.1
upper limit	-1.4
Variability estimate	Standard error of the mean
Dispersion value	0.18

Notes:

[59] - P-value was calculated by MMRM with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
Week 20	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	466
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[60]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.7
upper limit	-1
Variability estimate	Standard error of the mean
Dispersion value	0.18

Notes:

[60] - P-value was calculated by MMRM with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
Week 20	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	346
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[61]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.3
upper limit	-1.5
Variability estimate	Standard error of the mean
Dispersion value	0.2

Notes:

[61] - P-value was calculated by MMRM with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
Week 24	
Comparison groups	Placebo v CTP-543 8 mg BID

Number of subjects included in analysis	466
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[62]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	-1.3
Variability estimate	Standard error of the mean
Dispersion value	0.19

Notes:

[62] - P-value was calculated by MMRM with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
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Statistical analysis description:

Week 24

Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	346
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[63]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-2.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.6
upper limit	-1.8
Variability estimate	Standard error of the mean
Dispersion value	0.2

Notes:

[63] - P-value was calculated by MMRM with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

### **Secondary: Percentage of Subjects Achieving at Least a 75% and 90% Relative Reduction in SALT Score From Baseline at Weeks 12 and 24**

End point title	Percentage of Subjects Achieving at Least a 75% and 90% Relative Reduction in SALT Score From Baseline at Weeks 12 and 24
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End point description:

SALT is a quantitative assessment of scalp hair loss with scores ranging in severity from 0 (no scalp hair loss) to a maximum of 100 (complete scalp hair loss). Percentage of subjects achieving at least a 75% and 90% relative reduction in SALT score from baseline at Weeks 12 and 24 are reported. Efficacy population included all subjects who were randomised in the study and dispensed study drug during the treatment period.

End point type	Secondary
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End point timeframe:

Baseline, Weeks 12, and 24

<b>End point values</b>	Placebo	CTP-543 8 mg BID	CTP-543 12 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	140	351	215	
Units: percentage of subjects				
number (not applicable)				
75% Relative Reduction: Week 12	0	8.8	17.7	
75% Relative Reduction: Week 24	0	28.6	40.0	
90% Relative Reduction: Week 12	0	3.4	10.0	
90% Relative Reduction: Week 24	0	19.2	32.0	

## Statistical analyses

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description: 75% Relative Reduction: Week 12	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	491
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[64]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.06
upper limit	0.12
Variability estimate	Standard error of the mean
Dispersion value	0.016

Notes:

[64] - P-value was calculated by mantel-haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description: 75% Relative Reduction: Week 12	
Comparison groups	Placebo v CTP-543 12 mg BID

Number of subjects included in analysis	355
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[65]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.12
upper limit	0.22
Variability estimate	Standard error of the mean
Dispersion value	0.026

Notes:

[65] - P-value was calculated by mantel-haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description: 75% Relative Reduction: Week 24	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	491
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[66]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.23
upper limit	0.33
Variability estimate	Standard error of the mean
Dispersion value	0.025

Notes:

[66] - P-value was calculated by mantel-haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description: 75% Relative Reduction: Week 24	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	355
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[67]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.38

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.32
upper limit	0.45
Variability estimate	Standard error of the mean
Dispersion value	0.033

Notes:

[67] - P-value was calculated by mantel-haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
90% Relative Reduction: Week 12	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	491
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0006 <sup>[68]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.02
upper limit	0.06
Variability estimate	Standard error of the mean
Dispersion value	0.01

Notes:

[68] - P-value was calculated by mantel-haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
90% Relative Reduction: Week 12	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	355
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[69]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.06
upper limit	0.14
Variability estimate	Standard error of the mean
Dispersion value	0.02



Notes:

[69] - P-value was calculated by mantel-haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
90% Relative Reduction: Week 24	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	491
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[70]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.15
upper limit	0.23
Variability estimate	Standard error of the mean
Dispersion value	0.022

Notes:

[70] - P-value was calculated by mantel-haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
90% Relative Reduction: Week 24	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	355
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[71]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.24
upper limit	0.37
Variability estimate	Standard error of the mean
Dispersion value	0.032

Notes:

[71] - P-value was calculated by mantel-haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

## Secondary: Change in the Brigham Eyebrow Tool for Alopecia (BETA) Scores From

**Baseline at Weeks 12 and 24**

End point title	Change in the Brigham Eyebrow Tool for Alopecia (BETA) Scores From Baseline at Weeks 12 and 24
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End point description:

BETA is a clinician-rated scale that assesses the total eyebrow hair present. The BETA score is calculated based on hair density and surface area of each individual eyebrow of the subject, ranging from 0 to 3, where 0= no eyebrow, 1= minimal eyebrow, 2= moderate eyebrow, and 3= normal eyebrow. The BETA score is the sum of the right and left eyebrow scores, ranging from 0 to 6. Higher scores indicate less hair loss of eyebrows. A positive CFB indicates less hair loss of eyebrows. Efficacy population included all subjects who were randomised in the study and dispensed study drug during the treatment period. Overall number of subjects analysed indicates the number of subjects with data available for analysis of this end point. Number of subjects analyzed indicates the number of subjects with data available for analysis at the specified timepoint.

End point type	Secondary
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End point timeframe:

Baseline, Weeks 12, and 24

End point values	Placebo	CTP-543 8 mg BID	CTP-543 12 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	83	204	132	
Units: score on a scale				
arithmetic mean (standard deviation)				
Baseline	1.7 (± 2.05)	1.2 (± 1.77)	1.4 (± 1.91)	
CFB at Week 12 (n= 76, 187, 123)	-0.2 (± 1.38)	0.8 (± 1.70)	1.1 (± 2.05)	
CFB at Week 24 (n= 72, 192, 118)	-0.2 (± 1.68)	1.6 (± 1.96)	1.8 (± 2.17)	

**Statistical analyses**

Statistical analysis title	Placebo vs CTP-543 8 mg BID
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Statistical analysis description:

Week 12

Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	287
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001 <sup>[72]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3
upper limit	1.2
Variability estimate	Standard error of the mean
Dispersion value	0.22

Notes:

[72] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
Week 12	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [73]
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	1.6
Variability estimate	Standard error of the mean
Dispersion value	0.23

Notes:

[73] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
Week 24	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	287
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [74]
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	1.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.2
upper limit	2.2
Variability estimate	Standard error of the mean
Dispersion value	0.24

Notes:

[74] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
Week 24	
Comparison groups	Placebo v CTP-543 12 mg BID

Number of subjects included in analysis	215
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[75]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	1.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.4
upper limit	2.4
Variability estimate	Standard error of the mean
Dispersion value	0.26

Notes:

[75] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

## Secondary: Change in the Brigham Eyelash Tool for Alopecia (BELA) Scores From Baseline at Weeks 12 and 24

End point title	Change in the Brigham Eyelash Tool for Alopecia (BELA) Scores From Baseline at Weeks 12 and 24
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End point description:

BELA is a clinician-rated scale that assesses the total eyelash hair present. The BELA is calculated based on distribution and grade values, ranging from 0 (no eyelashes) to 3 (full eyelashes). The BELA score is the sum of the individual scores for the left and right eyes, ranging from 0 to 6. Higher scores indicate less hair loss of eyelashes. A positive CFB indicates less hair loss of eyelashes. Efficacy population included all subjects who were randomised in the study and dispensed study drug during the treatment period. Overall number of subjects analysed indicates the number of subjects with data available for analysis of this end point. Number of subjects analysed indicates the number of subjects with data available for analysis at the specified timepoint.

End point type	Secondary
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End point timeframe:

Baseline, Weeks 12, and 24

End point values	Placebo	CTP-543 8 mg BID	CTP-543 12 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	86	219	150	
Units: score on a scale				
arithmetic mean (standard deviation)				
Baseline	1.5 (± 2.12)	1.4 (± 2.10)	1.7 (± 2.12)	
CFB at Week 12 (n= 84, 215, 145)	-0.1 (± 1.18)	0.9 (± 1.50)	1.3 (± 2.08)	
CFB at Week 24 (n= 78, 209, 138)	0.3 (± 1.30)	1.7 (± 1.99)	2.0 (± 2.28)	

## Statistical analyses

Statistical analysis title	Placebo vs CTP-543 8 mg BID
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Statistical analysis description:

Week 12

Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	305
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[76]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5
upper limit	1.3
Variability estimate	Standard error of the mean
Dispersion value	0.2

Notes:

[76] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
Week 12	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	236
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[77]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	1
upper limit	1.8
Variability estimate	Standard error of the mean
Dispersion value	0.22

Notes:

[77] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
Week 24	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	305
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[78]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	1.5

Confidence interval	
level	95 %
sides	2-sided
lower limit	1
upper limit	2
Variability estimate	Standard error of the mean
Dispersion value	0.24

Notes:

[78] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
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Statistical analysis description:

Week 24

Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	236
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [79]
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	1.9

Confidence interval

level	95 %
sides	2-sided
lower limit	1.4
upper limit	2.4
Variability estimate	Standard error of the mean
Dispersion value	0.26

Notes:

[79] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

## Secondary: Change in the SPRO Scale From Baseline at Weeks 12, 16, 20, and 24

End point title	Change in the SPRO Scale From Baseline at Weeks 12, 16, 20, and 24
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End point description:

SPRO is a questionnaire answered by the subject and designed to measure how satisfied alopecia areata subjects are with their hair at the time of the assessment. The responses range from 1 to 5: 1= very satisfied, 2= satisfied, 3= neither satisfied nor dissatisfied, 4= dissatisfied, and 5= very dissatisfied. Higher scores indicate the greater hair dissatisfaction. A negative CFB indicate the greater hair satisfaction. Efficacy population included all subjects who were randomised in the study and dispensed study drug during the treatment period. Overall number of subjects analysed indicates the number of subjects with data available for analysis of this end point. Number of subjects analysed indicates the number of subjects with data available for analysis at the specified timepoint.

End point type	Secondary
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End point timeframe:

Baseline, Weeks 12, 16, 20, and 24

End point values	Placebo	CTP-543 8 mg BID	CTP-543 12 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	137	329	209	
Units: score on a scale				
arithmetic mean (standard deviation)				
Baseline	4.5 (± 0.86)	4.5 (± 0.89)	4.5 (± 0.85)	
CFB at Week 12 (n=135, 329, 209)	-0.6 (± 1.15)	-1.3 (± 1.42)	-1.7 (± 1.36)	
CFB at Week 16 (n=133, 322, 204)	-0.4 (± 1.18)	-1.4 (± 1.44)	-1.8 (± 1.43)	
CFB at Week 20 (n=131, 318, 200)	-0.4 (± 1.14)	-1.4 (± 1.52)	-1.8 (± 1.52)	
CFB at Week 24 (n=128, 318, 200)	-0.3 (± 1.09)	-1.5 (± 1.54)	-1.9 (± 1.64)	

## Statistical analyses

Statistical analysis title	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
Week 12	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	466
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[80]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	-0.5
Variability estimate	Standard error of the mean
Dispersion value	0.12

Notes:

[80] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, and baseline value.

Statistical analysis title	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
Week 12	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	346
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[81]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.1

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	-0.8
Variability estimate	Standard error of the mean
Dispersion value	0.13

Notes:

[81] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, and baseline value.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
Week 16	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	466
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[82]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	-0.8
Variability estimate	Standard error of the mean
Dispersion value	0.12

Notes:

[82] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, and baseline value.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
Week 16	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	346
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[83]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.6
upper limit	-1.1
Variability estimate	Standard error of the mean
Dispersion value	0.13



Notes:

[83] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, and baseline value.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
Week 20	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	466
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [84]
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	-0.8
Variability estimate	Standard error of the mean
Dispersion value	0.13

Notes:

[84] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, and baseline value.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
Week 20	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	346
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [85]
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.7
upper limit	-1.2
Variability estimate	Standard error of the mean
Dispersion value	0.14

Notes:

[85] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, and baseline value.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
Week 24	
Comparison groups	Placebo v CTP-543 8 mg BID

Number of subjects included in analysis	466
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[86]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	-1
Variability estimate	Standard error of the mean
Dispersion value	0.13

Notes:

[86] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, and baseline value.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
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Statistical analysis description:

Week 24

Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	346
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[87]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.8
upper limit	-1.3
Variability estimate	Standard error of the mean
Dispersion value	0.14

Notes:

[87] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, and baseline value.

### **Secondary: Percentage of Subjects Achieving a $\geq 2$ -point Change From Baseline in the SPRO Scale at Weeks 12, 16, 20, and 24**

End point title	Percentage of Subjects Achieving a $\geq 2$ -point Change From Baseline in the SPRO Scale at Weeks 12, 16, 20, and 24
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End point description:

SPRO is a questionnaire answered by the subject and designed to measure how satisfied alopecia areata subjects are with their hair at the time of the assessment. The responses range from 1 to 5: 1= very satisfied, 2= satisfied, 3= neither satisfied nor dissatisfied, 4= dissatisfied, and 5= very dissatisfied. Efficacy population included all subjects who were randomised in the study and dispensed study drug during the treatment period.

End point type	Secondary
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End point timeframe:

Weeks 12, 16, 20, and 24

End point values	Placebo	CTP-543 8 mg BID	CTP-543 12 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	140	351	215	
Units: percentage of subjects				
number (not applicable)				
Week 12	20.7	44.7	53.1	
Week 16	14.3	48.1	53.9	
Week 20	13.7	47.5	57.5	
Week 24	12.5	49.1	58.0	

## Statistical analyses

Statistical analysis title	Placebo vs CTP-543 8 mg BID
Statistical analysis description: Week 12	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	491
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[88]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.17
upper limit	0.34
Variability estimate	Standard error of the mean
Dispersion value	0.044

Notes:

[88] - P-value was calculated by the Mantel-Haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

Statistical analysis title	Placebo vs CTP-543 12 mg BID
Statistical analysis description: Week 12	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	355
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[89]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.32

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.23
upper limit	0.42
Variability estimate	Standard error of the mean
Dispersion value	0.049

Notes:

[89] - P-value was calculated by the Mantel-Haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
Week 16	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	491
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[90]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.27
upper limit	0.42
Variability estimate	Standard error of the mean
Dispersion value	0.04

Notes:

[90] - P-value was calculated by the Mantel-Haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
Week 16	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	355
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[91]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3
upper limit	0.48
Variability estimate	Standard error of the mean
Dispersion value	0.045

Notes:

[91] - P-value was calculated by the Mantel-Haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
Week 20	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	491
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [92]
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.26
upper limit	0.42
Variability estimate	Standard error of the mean
Dispersion value	0.04

Notes:

[92] - P-value was calculated by the Mantel-Haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
Week 20	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	355
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [93]
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.34
upper limit	0.51
Variability estimate	Standard error of the mean
Dispersion value	0.045

Notes:

[93] - P-value was calculated by the Mantel-Haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
Week 24	
Comparison groups	Placebo v CTP-543 8 mg BID

Number of subjects included in analysis	491
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[94]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.29
upper limit	0.44
Variability estimate	Standard error of the mean
Dispersion value	0.039

Notes:

[94] - P-value was calculated by the Mantel-Haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
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Statistical analysis description:

Week 24

Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	355
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[95]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.35
upper limit	0.53
Variability estimate	Standard error of the mean
Dispersion value	0.045

Notes:

[95] - P-value was calculated by the Mantel-Haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

### **Secondary: Change in the Individual Items of the Hair Quality Patient Reported Outcome (QPRO) Scale From Baseline at Weeks 12, 16, 20, and 24**

End point title	Change in the Individual Items of the Hair Quality Patient Reported Outcome (QPRO) Scale From Baseline at Weeks 12, 16, 20, and 24
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End point description:

The QPRO questionnaire provides additional details on key attributes of hair and helps provide context to the SPRO response. The individual items of QPRO are: Satisfied thickness hair coverage (STHC); Satisfied evenness hair coverage (SEHC); How satisfied with your eyebrows (HSWYE); How satisfied with your eyelashes (HSWYEI), scored on a scale ranging from 1 to 5 where 1=very satisfied, 2=satisfied, 3=neither satisfied nor dissatisfied, 4=dissatisfied, 5=very dissatisfied. Higher scores indicate the greater dissatisfaction on hair quality. A negative CFB indicate the greater satisfaction on hair quality. Efficacy population included all subjects who were randomised in the study and dispensed study drug during the treatment period. Overall number of subjects analysed indicates the number of subjects with data available for analysis of this end point. Number of subjects analysed indicates the number of subjects with data available for analysis at the specified timepoint.

End point type	Secondary
End point timeframe:	
Baseline, Weeks 12, 16, 20, and 24	

End point values	Placebo	CTP-543 8 mg BID	CTP-543 12 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	137	329	209	
Units: score on a scale				
arithmetic mean (standard deviation)				
STHC: Baseline	4.5 (± 0.79)	4.6 (± 0.79)	4.5 (± 0.76)	
STHC: CFB at Week 12 (n=135, 329, 209)	-0.4 (± 0.98)	-1.1 (± 1.23)	-1.3 (± 1.17)	
STHC: CFB at Week 16 (n=133, 322, 204)	-0.3 (± 1.03)	-1.2 (± 1.28)	-1.5 (± 1.33)	
STHC: CFB at Week 20 (n=131, 318, 200)	-0.3 (± 0.98)	-1.3 (± 1.35)	-1.6 (± 1.36)	
STHC: CFB at Week 24 (n=128, 318, 200)	-0.2 (± 1.00)	-1.4 (± 1.43)	-1.7 (± 1.45)	
SEHC: Baseline	4.6 (± 0.67)	4.6 (± 0.76)	4.6 (± 0.68)	
SEHC: CFB at Week 12 (n=135, 329, 209)	-0.4 (± 0.83)	-1.0 (± 1.19)	-1.3 (± 1.16)	
SEHC: CFB at Week 16 (n=133, 322, 204)	-0.3 (± 0.84)	-1.1 (± 1.31)	-1.4 (± 1.34)	
SEHC: CFB at Week 20 (n=131, 318, 200)	-0.3 (± 0.90)	-1.2 (± 1.36)	-1.5 (± 1.40)	
SEHC: CFB at Week 24 (n=128, 318, 200)	-0.2 (± 0.84)	-1.2 (± 1.41)	-1.6 (± 1.52)	
HSWYE: Baseline	3.8 (± 1.39)	4.0 (± 1.28)	3.9 (± 1.35)	
HSWYE: CFB at Week 12 (n=135, 329, 209)	-0.2 (± 0.88)	-1.0 (± 1.20)	-1.1 (± 1.34)	
HSWYE: CFB at Week 16 (n=133, 322, 204)	-0.1 (± 0.90)	-1.1 (± 1.24)	-1.3 (± 1.27)	
HSWYE: CFB at Week 20 (n=131, 318, 200)	-0.2 (± 0.88)	-1.2 (± 1.25)	-1.4 (± 1.32)	
HSWYE: CFB at Week 24 (n=128, 318, 200)	-0.2 (± 0.87)	-1.2 (± 1.26)	-1.4 (± 1.36)	
HSWYEI: Baseline	3.7 (± 1.44)	3.9 (± 1.37)	3.7 (± 1.44)	
HSWYEI: CFB at Week 12 (n=135, 329, 209)	-0.3 (± 0.79)	-0.9 (± 1.21)	-0.9 (± 1.24)	
HSWYEI: CFB at Week 16 (n=133, 322, 204)	-0.2 (± 0.97)	-1.0 (± 1.24)	-1.2 (± 1.30)	
HSWYEI: CFB at Week 20 (n=131, 318, 200)	-0.3 (± 0.99)	-1.1 (± 1.30)	-1.1 (± 1.33)	
HSWYEI: CFB at Week 24 (n=128, 318, 200)	-0.2 (± 0.95)	-1.1 (± 1.37)	-1.2 (± 1.37)	

## Statistical analyses

Statistical analysis title	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
STHC: Week 12	

Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	466
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[96]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	-0.5
Variability estimate	Standard error of the mean
Dispersion value	0.11

Notes:

[96] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
STHC: Week 12	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	346
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[97]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	-0.7
Variability estimate	Standard error of the mean
Dispersion value	0.12

Notes:

[97] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
STHC: Week 16	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	466
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[98]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-0.9



Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	-0.6
Variability estimate	Standard error of the mean
Dispersion value	0.12

Notes:

[98] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
STHC: Week 16	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	346
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[99]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	-1
Variability estimate	Standard error of the mean
Dispersion value	0.13

Notes:

[99] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
STHC: Week 20	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	466
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[100]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	-0.8
Variability estimate	Standard error of the mean
Dispersion value	0.12

Notes:

[100] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
STHC: Week 20	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	346
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[101]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.6
upper limit	-1.1
Variability estimate	Standard error of the mean
Dispersion value	0.13

Notes:

[101] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
STHC: Week 24	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	466
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[102]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	-0.8
Variability estimate	Standard error of the mean
Dispersion value	0.13

Notes:

[102] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
STHC: Week 24	
Comparison groups	Placebo v CTP-543 12 mg BID

Number of subjects included in analysis	346
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[103]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.7
upper limit	-1.2
Variability estimate	Standard error of the mean
Dispersion value	0.14

Notes:

[103] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
SEHC: Week 12	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	466
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[104]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	-0.4
Variability estimate	Standard error of the mean
Dispersion value	0.1

Notes:

[104] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
SEHC: Week 12	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	346
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[105]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-0.9

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	-0.7
Variability estimate	Standard error of the mean
Dispersion value	0.11

Notes:

[105] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
SEHC: Week 16	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	466
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[106]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	-0.5
Variability estimate	Standard error of the mean
Dispersion value	0.11

Notes:

[106] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
SEHC: Week 16	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	346
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[107]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	-0.8
Variability estimate	Standard error of the mean
Dispersion value	0.12

Notes:

[107] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
SEHC: Week 20	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	466
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[108]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	-0.7
Variability estimate	Standard error of the mean
Dispersion value	0.12

Notes:

[108] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
SEHC: Week 20	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	346
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[109]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	-1
Variability estimate	Standard error of the mean
Dispersion value	0.13

Notes:

[109] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
SEHC: Week 24	
Comparison groups	Placebo v CTP-543 8 mg BID

Number of subjects included in analysis	466
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[110]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	-0.7
Variability estimate	Standard error of the mean
Dispersion value	0.12

Notes:

[110] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
SEHC: Week 24	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	346
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[111]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	-1
Variability estimate	Standard error of the mean
Dispersion value	0.13

Notes:

[111] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
HSWYE: Week 12	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	466
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[112]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-0.7

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	-0.5
Variability estimate	Standard error of the mean
Dispersion value	0.11

Notes:

[112] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
HSWYE: Week 12	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	346
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[113]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	-0.6
Variability estimate	Standard error of the mean
Dispersion value	0.12

Notes:

[113] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
HSWYE: Week 16	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	466
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[114]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	-0.7
Variability estimate	Standard error of the mean
Dispersion value	0.11

Notes:

[114] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
HSWYE: Week 16	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	346
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[115]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	-0.9
Variability estimate	Standard error of the mean
Dispersion value	0.12

Notes:

[115] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
HSWYE: Week 20	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	466
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[116]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	-0.7
Variability estimate	Standard error of the mean
Dispersion value	0.11

Notes:

[116] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
HSWYE: Week 20	
Comparison groups	Placebo v CTP-543 12 mg BID



Number of subjects included in analysis	346
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[117]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	-0.9
Variability estimate	Standard error of the mean
Dispersion value	0.12

Notes:

[117] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
HSWYE: Week 24	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	466
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[118]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	-0.8
Variability estimate	Standard error of the mean
Dispersion value	0.11

Notes:

[118] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
HSWYE: Week 24	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	346
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[119]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.2

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	-0.9
Variability estimate	Standard error of the mean
Dispersion value	0.12

Notes:

[119] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
HSWYEL: Week 12	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	466
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[120]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	-0.3
Variability estimate	Standard error of the mean
Dispersion value	0.1

Notes:

[120] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
HSWYEL: Week 12	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	346
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[121]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	-0.4
Variability estimate	Standard error of the mean
Dispersion value	0.11

Notes:

[121] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

Statistical analysis title	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
HSWEI: Week 16	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	466
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[122]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	-0.5
Variability estimate	Standard error of the mean
Dispersion value	0.11

Notes:

[122] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

Statistical analysis title	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
HSWEI: Week 16	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	346
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[123]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	-0.7
Variability estimate	Standard error of the mean
Dispersion value	0.12

Notes:

[123] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

Statistical analysis title	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
HSWEI: Week 20	
Comparison groups	Placebo v CTP-543 8 mg BID

Number of subjects included in analysis	466
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[124]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	-0.5
Variability estimate	Standard error of the mean
Dispersion value	0.11

Notes:

[124] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
HSWEI: Week 20	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	346
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[125]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	-0.5
Variability estimate	Standard error of the mean
Dispersion value	0.12

Notes:

[125] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
HSWEI: Week 24	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	466
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[126]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-0.9

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	-0.6
Variability estimate	Standard error of the mean
Dispersion value	0.12

Notes:

[126] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
HSWEI: Week 24	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	346
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[127]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	-0.7
Variability estimate	Standard error of the mean
Dispersion value	0.13

Notes:

[127] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

### **Secondary: Change in the Anxiety and Depression Scale Scores of the Hospital Anxiety and Depression Scale (HADS) From Baseline at Week 24**

End point title	Change in the Anxiety and Depression Scale Scores of the Hospital Anxiety and Depression Scale (HADS) From Baseline at Week 24
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End point description:

HADS is questionnaire designed to assess anxiety and depression symptoms which is completed by subjects. The questionnaire is comprised of two separate scales with a total of 14 items: A 7-item scale related to anxiety and 7-item scale related to depression. Each item within both scales is scored using a 4-point scale, ranging from 0 to 3 and the total scores in each scale can range from 0 to 21. Separate scores were created for anxiety and depression. A score between 0-7 is considered normal, 8-10 is mild, 11-14 is moderate, and >14 is severe anxiety or depression. Higher scores indicate greater severity. A negative CFB indicates less severity. Efficacy population=all subjects who were randomised in the study and dispensed study drug during the treatment period. Overall number of subjects analysed=number of subjects with data available for analysis of this end point. Number of subjects analysed= number of subjects with data available for analysis at the specified timepoint.

End point type	Secondary
End point timeframe:	
Baseline and Week 24	

End point values	Placebo	CTP-543 8 mg BID	CTP-543 12 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	128	318	200	
Units: score on a scale				
arithmetic mean (standard deviation)				
Anxiety: Baseline	5.5 ( $\pm$ 3.92)	6.2 ( $\pm$ 4.06)	6.0 ( $\pm$ 3.92)	
Anxiety: CFB at Week 24	-0.4 ( $\pm$ 2.98)	-1.0 ( $\pm$ 3.26)	-1.1 ( $\pm$ 3.24)	
Depression: Baseline	3.3 ( $\pm$ 3.06)	3.7 ( $\pm$ 3.31)	3.6 ( $\pm$ 3.39)	
Depression: CFB at Week 24	-0.7 ( $\pm$ 2.67)	-0.9 ( $\pm$ 2.93)	-1.1 ( $\pm$ 2.88)	

## Statistical analyses

Statistical analysis title	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
Anxiety	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	446
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2489 <sup>[128]</sup>
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	0.9
Variability estimate	Standard error of the mean
Dispersion value	0.3

Notes:

[128] - P-value was calculated by analysis of covariance (ANCOVA) analysis with effects for treatment, visit, baseline SALT score, and baseline HADS value.

Statistical analysis title	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
Anxiety	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	328
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1235 <sup>[129]</sup>
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.5

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	1.1
Variability estimate	Standard error of the mean
Dispersion value	0.32

Notes:

[129] - P-value was calculated by ANCOVA analysis with effects for treatment, visit, baseline SALT score, and baseline HADS value.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
Depression	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	446
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9765 <sup>[130]</sup>
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	0.5
Variability estimate	Standard error of the mean
Dispersion value	0.25

Notes:

[130] - P-value was calculated by ANCOVA analysis with effects for treatment, visit, baseline SALT score, and baseline HADS value.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
Depression	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	328
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3559 <sup>[131]</sup>
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	0.8
Variability estimate	Standard error of the mean
Dispersion value	0.27

Notes:

[131] - P-value was calculated by ANCOVA analysis with effects for treatment, visit, baseline SALT score, and baseline HADS value.

## Secondary: Percentage of Subjects Achieving an Absolute SALT Score of $\leq 10$ at Week 24

End point title	Percentage of Subjects Achieving an Absolute SALT Score of $\leq 10$ at Week 24
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End point description:

SALT is a quantitative assessment of scalp hair loss with scores ranging in severity from 0 (no scalp hair loss) to a maximum of 100 (complete scalp hair loss). Efficacy population included all subjects who were randomised in the study and dispensed study drug during the treatment period.

End point type	Secondary
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End point timeframe:

Week 24

End point values	Placebo	CTP-543 8 mg BID	CTP-543 12 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	140	351	215	
Units: percentage of subjects				
number (not applicable)	0	20.8	34.5	

## Statistical analyses

Statistical analysis title	Placebo vs CTP-543 8 mg BID
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	491
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[132]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.16
upper limit	0.25
Variability estimate	Standard error of the mean
Dispersion value	0.022

Notes:

[132] - P-value was calculated by the Mantel-Haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

Statistical analysis title	Placebo vs CTP-543 12 mg BID
Comparison groups	Placebo v CTP-543 12 mg BID



Number of subjects included in analysis	355
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[133]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.27
upper limit	0.39
Variability estimate	Standard error of the mean
Dispersion value	0.032

Notes:

[133] - P-value was calculated by the Mantel-Haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

All-cause mortality: Randomisation up to Week 28; Adverse events: From first dose of study drug up to last follow up visit (Week 28)

Adverse event reporting additional description:

All-cause mortality: All randomised subjects included all subjects who were randomised in the study.  
Adverse events: Safety population included all subjects who received study drug during the treatment period.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
Dictionary version	23.1

### Reporting groups

Reporting group title	Placebo
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Reporting group description:

Subjects received CTP-543 matched placebo tablets, orally, BID for up to 24 weeks.

Reporting group title	CTP-543 8 mg BID
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Reporting group description:

Subjects received CTP-543 8 mg tablets, orally, BID for up to 24 weeks.

Reporting group title	CTP-543 12 mg BID
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Reporting group description:

Subjects received CTP-543 12 mg tablets, orally, BID for up to 24 weeks.

Serious adverse events	Placebo	CTP-543 8 mg BID	CTP-543 12 mg BID
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 140 (2.86%)	4 / 350 (1.14%)	1 / 215 (0.47%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Nervous system disorders			
Epilepsy			
subjects affected / exposed	1 / 140 (0.71%)	0 / 350 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	1 / 140 (0.71%)	0 / 350 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration			

site conditions			
Chest pain			
subjects affected / exposed	0 / 140 (0.00%)	1 / 350 (0.29%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 140 (0.00%)	1 / 350 (0.29%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Ileus			
subjects affected / exposed	0 / 140 (0.00%)	0 / 350 (0.00%)	1 / 215 (0.47%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 140 (0.00%)	1 / 350 (0.29%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Adjustment disorder			
subjects affected / exposed	1 / 140 (0.71%)	0 / 350 (0.00%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 140 (0.71%)	1 / 350 (0.29%)	1 / 215 (0.47%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	0 / 140 (0.00%)	1 / 350 (0.29%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis			

subjects affected / exposed	0 / 140 (0.00%)	1 / 350 (0.29%)	0 / 215 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 5 %

<b>Non-serious adverse events</b>	Placebo	CTP-543 8 mg BID	CTP-543 12 mg BID
Total subjects affected by non-serious adverse events			
subjects affected / exposed	31 / 140 (22.14%)	117 / 350 (33.43%)	75 / 215 (34.88%)
Investigations			
Blood creatine phosphokinase (increased)			
subjects affected / exposed	2 / 140 (1.43%)	21 / 350 (6.00%)	11 / 215 (5.12%)
occurrences (all)	2	21	11
Nervous system disorders			
Headache			
subjects affected / exposed	8 / 140 (5.71%)	41 / 350 (11.71%)	24 / 215 (11.16%)
occurrences (all)	8	41	24
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	7 / 140 (5.00%)	31 / 350 (8.86%)	26 / 215 (12.09%)
occurrences (all)	7	31	26
Infections and infestations			
COVID-19			
subjects affected / exposed	8 / 140 (5.71%)	19 / 350 (5.43%)	15 / 215 (6.98%)
occurrences (all)	8	19	15
Nasopharyngitis			
subjects affected / exposed	5 / 140 (3.57%)	18 / 350 (5.14%)	8 / 215 (3.72%)
occurrences (all)	5	18	8
Upper respiratory tract infection			
subjects affected / exposed	9 / 140 (6.43%)	9 / 350 (2.57%)	8 / 215 (3.72%)
occurrences (all)	9	9	8

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 August 2020	<ul style="list-style-type: none"><li>• Clarified contraception language to state "confirmed infertility".</li><li>• Clarified inclusion of subjects previously treated with a JAK inhibitor was at the discretion of the principal investigator, with consultation with the medical monitor if tolerability questions arose.</li><li>• Amended vital sign collection to allow for contactless monitoring of subject temperature.</li><li>• Removed the word "coverage" from question 1 and question 2 of the QPRO.</li></ul>
15 October 2020	<ul style="list-style-type: none"><li>• Removed stratification restriction to enable the study to cover the overall eligible subject population.</li><li>• Adjusted the original randomization ratio (3:3:1) to 3:5:2 due to re-evaluation of power calculations.</li><li>• Distinguished treatment withdrawal from study withdrawal.</li><li>• Removed the exclusion criterion "Atypical nevi or cutaneous lesions that are suspicious for malignancy".</li><li>• Adjusted the efficacy evaluation by adding Week 8 to the key secondary endpoints for SALT score assessment and adding Week 16 and 20 to secondary endpoints for CGI/PGI.</li><li>• Added collection time points for ECG (added Week 12), PGI-I/CGI-I (added Week 16 and Week 20), and PGI-S/CGI-S (added Week 16 and Week 20).</li><li>• Added evaluation for progressive multifocal leukoencephalopathy (PML) and presence or absence of nasal hairs during physical exams.</li><li>• Updated statistical analyses to reflect modifications to primary endpoint analysis, missing data, adjustment for multiplicity, and tipping point analysis.</li></ul>
08 October 2021	<ul style="list-style-type: none"><li>• Coordinating investigator contact information updated.</li></ul>

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported