Clinical trial results:
A Phase 2, multicenter, prospective, randomized, double-blind, Minoxidil and vehicle controlled, dose-ranging study to evaluate the efficacy and safety of CB-03-01 (Cortexolone 17-propionate) solution for the treatment of androgenetic alopecia in females

Summary

EudraCT number	2019-000950-78
Trial protocol	DE
Global end of trial date	21 April 2021

Results information

Result version number	v1 (current)
This version publication date	25 October 2022
First version publication date	25 October 2022

Trial information

Trial identification

Sponsor protocol code	CB-03-01/35

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Cassiopea S.p.A:
Sponsor organisation address	Via C. Colombo, 1, Lainate/Milan, Italy, 20045
Public contact	R&D Department, Cassiopea S.p.A., +39 0286891124, dermatology@cosmopharma.com
Scientific contact	R&D Department, Cassiopea S.p.A., +39 0286891124, dermatology@cosmopharma.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	21 April 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 April 2021
Global end of trial reached?	Yes
Global end of trial date	21 April 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of this study is to evaluate the efficacy and safety of Clascoterone (CB-03-01) topical solution 5% and 7.5% BID (twice a day) dosing compared to the Minoxidil solution 2% (BID) and the vehicle solution (BID) for the treatment of androgenetic alopecia (AGA) in females.

Protection of trial subjects:

Before being admitted to the study the subjects were informed in detail about the significance, nature, scope and possible risks of the study. Written information was available for this purpose.
Subjects were free to terminate their participation in the study at any time without personal disadvantages and without giving reasons. The subjects were informed that all study data would have been collected and stored in an electronic database, pseudoanonymized, and handled in the strictest confidence.
Randomized subjects were provided with instruction sheet, diary and study subject cards indicating the nature of the trial the subject is participating, contact details and any information needed in the event of a medical emergency.

Background therapy:

No background therapy foreseen in this study.

Evidence for comparator:

Minoxidil was used as comparator being an available treatment on the market for the AGA

Actual start date of recruitment	20 November 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 293
Worldwide total number of subjects	293
EEA total number of subjects	293

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)	293
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was carried out at seven study centers in Germany. A total of 329 subjects were screened and 293 randomized. The enrolment/randomization period included about 10 months instead of the planned 6 months as there was a temporary recruitment halt of about two months due to the COVID-19 pandemic.

Pre-assignment

Screening details:

Eligible subjects were adult (18 to 55 years of age) females who had to show and had a history of hair density reduction in the centroparietal region, as classified by the Savin Density Scale.
The screening period ranged from Day -14 to -3. A washout phase from prohibited medications or treatments was foreseen, if necessary.

Period 1

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

Blinding implementation details:

The various concentrations of CB-03-01 solution, Minoxidil and vehicle solution were packaged in identical 60 ml glass amber bottles and the treatment was randomly assigned to the subjects through a centralized randomization list.Treatment group designation at the site level remained blinded until the final database was locked.
Sealed Emergency Unblinding Forms were available for each kit at the study sites for emergency unblinding.

Arms

Are arms mutually exclusive?	Yes
Arm title	CB-03-01 solution, 5%

Arm description:

Clascoterone (CB-03-01) solution, 5% BID

Arm type	Experimental
Investigational medicinal product name	Clascoterone solution 5%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cutaneous solution
Routes of administration	Topical use

Dosage and administration details:

1mL of solution applied to the balding areas of the scalp (centroparietal region) twice daily over a period of 6 months

Arm title	CB-03-01 solution, 7.5%

Arm description:

Clascoterone (CB-03-01) solution 7.5% BID

Arm type	Experimental
Investigational medicinal product name	Clascoterone solution 7.5%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cutaneous solution
Routes of administration	Topical use

Dosage and administration details:

1mL of solution applied to the balding areas of the scalp (centroparietal region) twice daily over a period

of 6 months

Arm title	Minoxidil solution, 2%
Arm description:	
Minoxidil solution 2% BID	
Arm type	Experimental
Investigational medicinal product name	Minixidil solution 2%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cutaneous solution
Routes of administration	Topical use
Dosage and administration details:	
1mL of solution applied to the balding areas of the scalp (centroparietal region) twice daily over a period of 6 months	

Arm title	Vehicle solution
Arm description:	
Clascoterone Vehicle solution BID (twice a day)	
Arm type	Placebo
Investigational medicinal product name	Vehicle solution
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cutaneous solution
Routes of administration	Topical use
Dosage and administration details:	
1mL of solution applied to the balding areas of the scalp (centroparietal region) twice daily over a period of 6 months	

Number of subjects in period 1	CB-03-01 solution, 5%	CB-03-01 solution, 7.5%	Minoxidil solution, 2%
Started	72	73	75
Completed	62	66	70
Not completed	10	7	5
Consent withdrawn by subject	3	1	2
Adverse event, non-fatal	3	3	2
Other	1	3	1
Pregnancy	1	-	-
Lost to follow-up	2	-	-

Number of subjects in period 1	Vehicle solution
Started	73
Completed	68
Not completed	5
Consent withdrawn by subject	1

Adverse event, non-fatal	-
Other	4
Pregnancy	-
Lost to follow-up	-

Baseline characteristics

Reporting groups	
Reporting group title	CB-03-01 solution, 5%
Reporting group description: Clascoterone (CB-03-01) solution, 5% BID	
Reporting group title	CB-03-01 solution, 7.5%
Reporting group description: Clascoterone (CB-03-01) solution 7.5% BID	
Reporting group title	Minoxidil solution, 2%
Reporting group description: Minoxidil solution 2% BID	
Reporting group title	Vehicle solution
Reporting group description: Clascoterone Vehicle solution BID (twice a day)	

Reporting group values	CB-03-01 solution, 5%	CB-03-01 solution, 7.5%	Minoxidil solution, 2%
Number of subjects	72	73	75
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	72	73	75
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	40.3	40.5	39.9
standard deviation	± 11.4	± 10.5	± 10.4
Gender categorical Units: Subjects			
Female	72	73	75
Male	0	0	0
Ethnicity Units: Subjects			
Hispanic or Latino	1	0	0
Not Hispanic or Latino	71	73	75
Race Units: Subjects			
White	67	73	74
Asian	3	0	1
African American	0	0	0
Other	2	0	0

Savin Density Scale			
The Savin scale measures overall thinning of the crown scalp and consists of eight crown density images reflecting a range from no hair loss to severe hair loss (Density stages picture nos. 1, 2, 3, 4, 5, 6, 7, and 8). Eligible for this study were only subjects being classified having stage picture nos. 3–6 .			
Units: Subjects			
Stage 3	30	27	39
Stage 4	24	34	27
Stage 5	14	11	7
Stage 6	4	1	2
Postmenopausal hormonal status Units: Subjects			
No	55	60	57
Yes	17	13	18

Reporting group values	Vehicle solution	Total	
Number of subjects	73	293	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	73	293	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	41.8		
standard deviation	± 9.8	-	
Gender categorical Units: Subjects			
Female	73	293	
Male	0	0	
Ethnicity Units: Subjects			
Hispanic or Latino	3	4	
Not Hispanic or Latino	70	289	
Race Units: Subjects			
White	71	285	
Asian	1	5	
African American	1	1	
Other	0	2	
Savin Density Scale			
The Savin scale measures overall thinning of the crown scalp and consists of eight crown density images reflecting a range from no hair loss to severe hair loss (Density stages picture nos. 1, 2, 3, 4, 5, 6, 7, and 8). Eligible for this study were only subjects being classified having stage picture nos. 3–6 .			
Units: Subjects			

Stage 3	30	126	
Stage 4	32	117	
Stage 5	11	43	
Stage 6	0	7	
Postmenopausal hormonal status Units: Subjects			
No	58	230	
Yes	15	63	

Subject analysis sets

Subject analysis set title	Efficay Population - CB-03-01 solution, 5%
Subject analysis set type	Per protocol
Subject analysis set description: Subjects treated with CB-03-01 solution 5% and included in the PP population	
Subject analysis set title	Efficay Population - CB-03-01 solution, 7.5%
Subject analysis set type	Per protocol
Subject analysis set description: Subjects treated with CB-03-01 solution 7.5% and included in the PP population	
Subject analysis set title	Efficay Population - Minoxidil solution, 2%
Subject analysis set type	Per protocol
Subject analysis set description: Subjects treated with Minoxidil solution, 2% and included in the PP population	
Subject analysis set title	Efficay Population - Vehicle solution
Subject analysis set type	Per protocol
Subject analysis set description: Subjects treated with vehicle solution and included in the PP population	

Reporting group values	Efficay Population - CB-03-01 solution, 5%	Efficay Population - CB-03-01 solution, 7.5%	Efficay Population - Minoxidil solution, 2%
Number of subjects	61	65	66
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	61	65	66
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	40.3	40.1	39.9
standard deviation	± 11.3	± 10.5	± 10.2
Gender categorical Units: Subjects			
Female	61	65	66
Male			

Ethnicity Units: Subjects			
Hispanic or Latino	1	0	0
Not Hispanic or Latino	60	65	66
Race Units: Subjects			
White	58	65	65
Asian	2	0	1
African American	0	0	0
Other	1	0	0
Savin Density Scale			
The Savin scale measures overall thinning of the crown scalp and consists of eight crown density images reflecting a range from no hair loss to severe hair loss (Density stages picture nos. 1, 2, 3, 4, 5, 6, 7, and 8). Eligible for this study were only subjects being classified having stage picture nos. 3–6 .			
Units: Subjects			
Stage 3	25	23	35
Stage 4	21	30	24
Stage 5	12	11	5
Stage 6	3	1	2
Postmenopausal hormonal status Units: Subjects			
No	47	54	51
Yes	14	11	15

Reporting group values	Efficay Population - Vehicle solution		
Number of subjects	64		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	64		
From 65-84 years	0		
85 years and over	0		
Age continuous Units: years			
arithmetic mean	42.6		
standard deviation	± 9.6		
Gender categorical Units: Subjects			
Female	64		
Male			
Ethnicity Units: Subjects			
Hispanic or Latino	0		
Not Hispanic or Latino	64		

Race Units: Subjects			
White	63		
Asian	0		
African American	1		
Other	0		
Savin Density Scale			
The Savin scale measures overall thinning of the crown scalp and consists of eight crown density images reflecting a range from no hair loss to severe hair loss (Density stages picture nos. 1, 2, 3, 4, 5, 6, 7, and 8). Eligible for this study were only subjects being classified having stage picture nos. 3–6 .			
Units: Subjects			
Stage 3	27		
Stage 4	28		
Stage 5	9		
Stage 6	0		
Postmenopausal hormonal status Units: Subjects			
No	49		
Yes	15		

End points

End points reporting groups

Reporting group title	CB-03-01 solution, 5%
Reporting group description: Clascoterone (CB-03-01) solution, 5% BID	
Reporting group title	CB-03-01 solution, 7.5%
Reporting group description: Clascoterone (CB-03-01) solution 7.5% BID	
Reporting group title	Minoxidil solution, 2%
Reporting group description: Minoxidil solution 2% BID	
Reporting group title	Vehicle solution
Reporting group description: Clascoterone Vehicle solution BID (twice a day)	
Subject analysis set title	Efficay Population - CB-03-01 solution, 5%
Subject analysis set type	Per protocol
Subject analysis set description: Subjects treated with CB-03-01 solution 5% and included in the PP population	
Subject analysis set title	Efficay Population - CB-03-01 solution, 7.5%
Subject analysis set type	Per protocol
Subject analysis set description: Subjects treated with CB-03-01 solution 7.5% and included in the PP population	
Subject analysis set title	Efficay Population - Minoxidil solution, 2%
Subject analysis set type	Per protocol
Subject analysis set description: Subjects treated with Minoxidil solution, 2% and included in the PP population	
Subject analysis set title	Efficay Population - Vehicle solution
Subject analysis set type	Per protocol
Subject analysis set description: Subjects treated with vehicle solution and included in the PP population	

Primary: Non-vellus TAHC – Change from Baseline at Month 6 for active treatment groups in comparison to vehicle group – PP

End point title	Non-vellus TAHC – Change from Baseline at Month 6 for active treatment groups in comparison to vehicle group – PP
End point description:	
End point type	Primary
End point timeframe: From baseline to month 6	

End point values	Efficay Population - CB-03-01 solution, 5%	Efficay Population - CB-03-01 solution, 7.5%	Efficay Population - Minoxidil solution, 2%	Efficay Population - Vehicle solution
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	61	65	66	64
Units: TAHC				
number (confidence interval 95%)	7.1 (4.0 to 10.1)	2.8 (-0.5 to 6.2)	18.2 (13.7 to 22.7)	9.1 (5.2 to 12.9)

Statistical analyses

Statistical analysis title	Change from Baseline in non-vellus TAHC at Month 6

Statistical analysis description:

Non-vellus TAHC - Change from Baseline at Month 6 in comparison to vehicle was evaluated in PP by restricted maximum likelihood
(REML)-based MMRM (8) where the model includes treatment, visit, the treatment by visit interaction, and analysis center as factors and the baseline non-vellus TAHC and baseline non-vellus TAHC-by-visit interaction as the covariates. An unstructured covariance structure of within subject errors and the Kenward-Roger degrees of freedom approximation was used.

Comparison groups	Efficay Population - CB-03-01 solution, 5% v Efficay Population - CB-03-01 solution, 7.5% v Efficay Population - Minoxidil solution, 2% v Efficay Population - Vehicle solution
Number of subjects included in analysis	256
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	≤ 0.05
Method	paired t-test

Notes:

[1] - No confirmatory hypotheses were formulated for this exploratory study. The analyses were conducted without adjustment for multiplicity and were interpreted
descriptively. The covariance structure converging to the best fit, as determined by Akaike's information criterion, was used as the primary analysis. Pairwise comparisons for the LSM between the active treatments and the vehicle were evaluated. Within treatment group comparisons for non-vellus TAHC vs Baseline were based on paired t-test

Primary: Hair Growth Assessment (HGA) at Month 6 for active treatment groups in comparison to vehicle group - PP

End point title	Hair Growth Assessment (HGA) at Month 6 for active treatment groups in comparison to vehicle group - PP

End point description:

End point type	Primary

End point timeframe:

From baseline to month 6

End point values	Efficay Population - CB-03-01 solution, 5%	Efficay Population - CB-03-01 solution, 7.5%	Efficay Population - Minoxidil solution, 2%	Efficay Population - Vehicle solution
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	61	65	66	64
Units: HGA - Observed cases (OC)				
Hair growth increased	35	43	50	34
No change in hair growth	22	19	15	21
Hair growth decreased	4	3	1	9

Statistical analyses

Statistical analysis title	Hair Growth Assessment (HGA) at Month 6

Statistical analysis description:

The frequency distribution of HGA score at Month 6 was evaluated using a CMH mean score test stratified by analysis center using modified ridit score for between-group comparisons. Pairwise comparisons between the active treatment groups and vehicle were evaluated. If the tables were sparse, Fisher's Exact test might have been used or categories might have been collapsed for analysis.

Comparison groups	Efficay Population - CB-03-01 solution, 5% v Efficay Population - CB-03-01 solution, 7.5% v Efficay Population - Minoxidil solution, 2% v Efficay Population - Vehicle solution
Number of subjects included in analysis	256
Analysis specification	Pre-specified
Analysis type	other[2]
P-value	≤ 0.05
Method	Cochran-Mantel-Haenszel

Notes:

[2] - No confirmatory hypotheses were formulated for this exploratory study. The analyses specified in the following were conducted without adjustment for multiplicity and were interpreted descriptively.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Collection of information on the medical condition of subjects begun following the subject's written informed consent to participate in the study and ended at the date of the final study visit or later in case a fu was needed.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	CB-03-01 solution, 5%
Reporting group description:	
Clascoterone (CB-03-01) solution, 5% BID	
Reporting group title	CB-03-01 solution, 7.5%
Reporting group description:	
Clascoterone (CB-03-01) solution 7.5% BID	
Reporting group title	Minoxidil solution, 2%
Reporting group description:	
Minoxidil solution 2% BID	
Reporting group title	Vehicle solution
Reporting group description:	
Clascoterone Vehicle solution BID (twice a day)	

Serious adverse events	CB-03-01 solution, 5%	CB-03-01 solution, 7.5%	Minoxidil solution, 2%
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 72 (2.78%)	0 / 74 (0.00%)	0 / 74 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Nervous system disorders			
Migraine			
subjects affected / exposed	1 / 72 (1.39%)	0 / 74 (0.00%)	0 / 74 (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
Reproductive system and breast disorders			
Heavy menstrual bleeding			
subjects affected / exposed	1 / 72 (1.39%)	0 / 74 (0.00%)	0 / 74 (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

Serious adverse events	Vehicle solution		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 73 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Nervous system disorders			
Migraine			
subjects affected / exposed	0 / 73 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Heavy menstrual bleeding			
subjects affected / exposed	0 / 73 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	CB-03-01 solution, 5%	CB-03-01 solution, 7.5%	Minoxidil solution, 2%
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 72 (18.06%)	11 / 74 (14.86%)	25 / 74 (33.78%)
Investigations			
Blood thyroid stimulating hormone increased			
subjects affected / exposed	1 / 72 (1.39%)	0 / 74 (0.00%)	5 / 74 (6.76%)
occurrences (all)	1	0	5
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 72 (4.17%)	4 / 74 (5.41%)	6 / 74 (8.11%)
occurrences (all)	8	11	6
General disorders and administration site conditions			
Application site pruritus			
subjects affected / exposed	1 / 72 (1.39%)	2 / 74 (2.70%)	4 / 74 (5.41%)
occurrences (all)	1	2	4
Application site alopecia			

subjects affected / exposed	0 / 72 (0.00%)	1 / 74 (1.35%)	4 / 74 (5.41%)
occurrences (all)	0	1	4
Blood and lymphatic system disorders			
Iron deficiency anaemia			
subjects affected / exposed	0 / 72 (0.00%)	0 / 74 (0.00%)	0 / 74 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	8 / 72 (11.11%)	4 / 74 (5.41%)	6 / 74 (8.11%)
occurrences (all)	9	4	6

Non-serious adverse events	Vehicle solution		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 73 (19.18%)		
Investigations			
Blood thyroid stimulating hormone increased			
subjects affected / exposed	0 / 73 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
General disorders and administration site conditions			
Application site pruritus			
subjects affected / exposed	6 / 73 (8.22%)		
occurrences (all)	8		
Application site alopecia			
subjects affected / exposed	0 / 73 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Iron deficiency anaemia			
subjects affected / exposed	1 / 73 (1.37%)		
occurrences (all)	1		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	7 / 73 (9.59%)		
occurrences (all)	7		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported