Clinical trial results:
A PHASE 2, MULTICENTER, PROSPECTIVE, RANDOMIZED, DOUBLE-BLIND, 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 MALES

Summary

EudraCT number	2016-003733-23
Trial protocol	DE
Global end of trial date	06 January 2019

Results information

Result version number	v1 (current)
This version publication date	08 August 2020
First version publication date	08 August 2020

Trial information

Trial identification

Sponsor protocol code	CB-03-01/34

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 (MI), Italy, 20045
Public contact	R&D department, Cassiopea S.p.A., +39 0286891124,
Scientific contact	R&D department, Cassiopea S.p.A., +39 0286891124,

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	20 September 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 January 2019
Global end of trial reached?	Yes
Global end of trial date	06 January 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of the study was to evaluate the efficacy and safety of CB-03-01 solution, 2.5%, 5.0%, 7.5% BID (twice a day) dosing and 7.5% QD (once per day) dosing compared to vehicle for the treatment of androgenetic alopecia (AGA) in males.

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 be 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:

No comparator(s) used in this study.

Actual start date of recruitment	21 June 2017
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: 404
Worldwide total number of subjects	404
EEA total number of subjects	404

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)	404
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was carried out at six study centers in Germany. A total of 431 subjects were screened and 404 randomized. The randomization period included about 5 months. The first subject was randomized on 26JUN2017, the last subject on 01DEC2017. The study duration included about 18 months. The last subject completed the study on 06JAN2019.

Pre-assignment

Screening details:

Eligible subjects were adult (18 to 55 years of age) male affected by a mild to moderate AGA with a history of ongoing hair loss in the temple and vertex region, as classified by the Modified Norwood-Hamilton Scale. The screening period ranged from Day -14 to -3. A washout phase from prohibited medications or treatments was foreseen, if necessary.

Pre-assignment period milestones

Number of subjects started	431[1]
Number of subjects completed	404

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Failed eligibility criteria: 9
Reason: Number of subjects	Consent withdrawn by subject: 16
Reason: Number of subjects	Not specified: 2

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: the pre-assignment period is here considered as the inclusion of the subject in the screening phase of the study, so the number of subjects reported to have started the pre-assignment period is the number of subjects that were screened (Informed Consent form signed, subject study ID assigned and screening procedures started/performed).

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	Investigator, Monitor, Subject

Blinding implementation details:

The various concentrations of CB-03-01 solution and vehicle solution were packaged in identical 60 ml glass amber bottles and the treatment was randomly assigned to the subjects through an IWRS. 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, 2.5% BID

Arm description:

CB-03-01 solution, 2.5% BID (twice a day)

Arm type	Experimental

Investigational medicinal product name	CB-03-01 solution, 2.5%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cutaneous solution
Routes of administration	Topical use

Dosage and administration details:

1 mL applied to the balding areas of the scalp (vertex and temple) twice daily over a period of 12 months

Arm title	CB-03-01 solution, 5% BID

Arm description:

CB-03-01 solution, 5% BID (twice a day)

Arm type	Experimental
Investigational medicinal product name	CB-03-01 solution, 5%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cutaneous solution
Routes of administration	Topical use

Dosage and administration details:

1 mL applied to the balding areas of the scalp (vertex and temple) twice daily over a period of 12 months

Arm title	CB-03-01 solution 7.5% BID

Arm description:

CB-03-01 solution 7.5% BID (twice a day)

Arm type	Experimental
Investigational medicinal product name	CB-03-01 solution, 7.5%
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cutaneous solution
Routes of administration	Topical use

Dosage and administration details:

1 mL applied to the balding areas of the scalp (vertex and temple) twice daily over a period of 12 months

Arm title	CB-03-01 solution, 7.5% QD/vehicle solution QD

Arm description:

CB-03-01 solution, 7.5% QD (once per day) and vehicle solution QD (once per day)

Arm type	Experimental
Investigational medicinal product name	CB-03-01 solution, 7.5% QD/ vehicle solution QD
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cutaneous solution
Routes of administration	Topical use

Dosage and administration details:

1 mL applied to the balding areas of the scalp (vertex and temple) twice daily over a period of 12 months

Arm title	Vehicle solution BID

Arm description:

Vehicle solution BID (twice a day)

Arm type	Placebo

Investigational medicinal product name	Vehicle solution BID
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Cutaneous solution
Routes of administration	Topical use

Dosage and administration details:

1 mL applied to the balding areas of the scalp (vertex and temple) twice daily over a period of 12 months

Number of subjects in period 1	CB-03-01 solution, 2.5% BID	CB-03-01 solution, 5% BID	CB-03-01 solution 7.5% BID
Started	82	78	82
Completed	78	68	70
Not completed	4	10	12
Consent withdrawn by subject	3	5	5
Adverse event, non-fatal	1	4	1
Not specified	-	-	1
Lost to follow-up	-	1	4
Protocol deviation	-	-	1
Lack of efficacy	-	-	-

Number of subjects in period 1	CB-03-01 solution, 7.5% QD/vehicle solution QD	Vehicle solution BID
Started	80	82
Completed	71	73
Not completed	9	9
Consent withdrawn by subject	5	3
Adverse event, non-fatal	1	4
Not specified	-	-
Lost to follow-up	2	2
Protocol deviation	-	-
Lack of efficacy	1	-

Baseline characteristics

Reporting groups	
Reporting group title	CB-03-01 solution, 2.5% BID
Reporting group description:	
CB-03-01 solution, 2.5% BID (twice a day)	
Reporting group title	CB-03-01 solution, 5% BID
Reporting group description:	
CB-03-01 solution, 5% BID (twice a day)	
Reporting group title	CB-03-01 solution 7.5% BID
Reporting group description:	
CB-03-01 solution 7.5% BID (twice a day)	
Reporting group title	CB-03-01 solution, 7.5% QD/vehicle solution QD
Reporting group description:	
CB-03-01 solution, 7.5% QD (once per day) and vehicle solution QD (once per day)	
Reporting group title	Vehicle solution BID
Reporting group description:	
Vehicle solution BID (twice a day)	

Reporting group values	CB-03-01 solution, 2.5% BID	CB-03-01 solution, 5% BID	CB-03-01 solution 7.5% BID
Number of subjects	82	78	82
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	39.9	41.2	39.3
standard deviation	± 9.71	± 9.58	± 9.67
Gender categorical Units: Subjects			
Female	0	0	0
Male	82	78	82
Ethnicity Units: Subjects			
Hispanic or Latino	1	3	6
Not Hispanic or Latino	81	75	76
Modified Norwood-hamilton Scale Units: Subjects			
Type III Vertex	32	25	36
Type IV	29	36	24
Type V	21	17	22

Reporting group values	CB-03-01 solution, 7.5% QD/vehicle solution QD	Vehicle solution BID	Total
Number of subjects	80	82	404
Age categorical Units: Subjects			

Age continuous Units: years			
arithmetic mean	39.8	39.2	
standard deviation	± 9.40	± 10.15	-
Gender categorical Units: Subjects			
Female	0	0	0
Male	80	82	404
Ethnicity Units: Subjects			
Hispanic or Latino	0	0	10
Not Hispanic or Latino	80	82	394
Modified Norwood-hamilton Scale Units: Subjects			
Type III Vertex	31	28	152
Type IV	34	34	157
Type V	15	20	95

End points

End points reporting groups

Reporting group title	CB-03-01 solution, 2.5% BID
Reporting group description: CB-03-01 solution, 2.5% BID (twice a day)	
Reporting group title	CB-03-01 solution, 5% BID
Reporting group description: CB-03-01 solution, 5% BID (twice a day)	
Reporting group title	CB-03-01 solution 7.5% BID
Reporting group description: CB-03-01 solution 7.5% BID (twice a day)	
Reporting group title	CB-03-01 solution, 7.5% QD/vehicle solution QD
Reporting group description: CB-03-01 solution, 7.5% QD (once per day) and vehicle solution QD (once per day)	
Reporting group title	Vehicle solution BID
Reporting group description: Vehicle solution BID (twice a day)	

Primary: Comparison of changes from baseline in non-vellus Target Area Hair Counts (TAHC) at Month 12

End point title	Comparison of changes from baseline in non-vellus Target Area Hair Counts (TAHC) at Month 12
End point description: Non-vellus TAHC: Comparison Month 12 vs Baseline - OC (PP Population). The change from Baseline in non-vellus TAHC at Month 12 was evaluated.	
End point type	Primary
End point timeframe: Month 12	

End point values	CB-03-01 solution, 2.5% BID	CB-03-01 solution, 5% BID	CB-03-01 solution 7.5% BID	CB-03-01 solution, 7.5% QD/vehicle solution QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	74	66	68	66
Units: Changes				
number (confidence interval 95%)	1.0 (-4.2 to 6.2)	4.4 (-1.4 to 10.2)	4.7 (-0.3 to 9.8)	3.5 (-2.7 to 9.8)

End point values	Vehicle solution BID			
Subject group type	Reporting group			
Number of subjects analysed	70			
Units: Changes				

number (confidence interval 95%)	-9.3 (-14.7 to -3.9)			

Statistical analyses

Statistical analysis title	Change from Baseline in non-vellus TAHC at month12

Statistical analysis description:

The change from Baseline in non-vellus TAHC at Month 12 was evaluated by analysis of covariance including in the model treatment, visit, 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. The covariance stucture converging to the best fit was used as the primary analysis.
Pairwise comparisons for the LSM between active treatment groups and the vehicle group were evaluated.

Comparison groups	CB-03-01 solution, 2.5% BID v CB-03-01 solution, 5% BID v CB-03-01 solution 7.5% BID v CB-03-01 solution, 7.5% QD/vehicle solution QD v Vehicle solution BID
Number of subjects included in analysis	344
Analysis specification	Pre-specified
Analysis type	superiority
P-value	≤ 0.05
Method	ANCOVA; paired t-test

Primary: Comparison of changes from baseline in non-vellus Target Area Hair Counts (TAHC) at Month 12 in active groups vs vehicle

End point title	Comparison of changes from baseline in non-vellus Target Area Hair Counts (TAHC) at Month 12 in active groups vs vehicle

End point description:

Non-vellus TAHC: comparison vs vehicle at Month 12 using MMRM - OC (PP population).
Changes from baseline for parameter Non-vellus TAHC - OC

End point type	Primary

End point timeframe:

Month 12

End point values	CB-03-01 solution, 2.5% BID	CB-03-01 solution, 5% BID	CB-03-01 solution 7.5% BID	CB-03-01 solution, 7.5% QD/vehicle solution QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	74	66	68	66
Units: changes				
number (confidence interval 95%)	10.2 (2.6 to 17.8)	13.8 (5.9 to 21.6)	14.3 (6.6 to 22.1)	12.7 (4.9 to 20.6)

End point values	Vehicle solution			

	BID			
Subject group type	Reporting group			
Number of subjects analysed	70			
Units: changes				
number (confidence interval 95%)	0 (0 to 0)			

Statistical analyses

Statistical analysis title	Non-vellus TAHC: comparison vs vehicle at Month 12

Statistical analysis description:

The change from Baseline in non-vellus TAHC at Month 12 was evaluated by analysis of covariance including in the model treatment, visit, 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. The covariance stucture converging to the best fit was used as the primary analysis.
Pairwise comparisons for the LSM between active treatment groups and the vehicle group were evaluated.

Comparison groups	CB-03-01 solution, 2.5% BID v CB-03-01 solution, 5% BID v CB-03-01 solution 7.5% BID v CB-03-01 solution, 7.5% QD/vehicle solution QD v Vehicle solution BID
Number of subjects included in analysis	344
Analysis specification	Pre-specified
Analysis type	superiority
P-value	≤ 0.05
Method	ANCOVA; unpaired t-test

Primary: Hair Grow Assesment (HGA) at Month 12

End point title	Hair Grow Assesment (HGA) at Month 12

End point description:

Hair Grow Assesment (HGA) Score at Month 12: Summary and Comparison - OC (PP Population).
The frequency distribution of HGA score at Month 12 was wvaluated.

End point type	Primary

End point timeframe:

Month 12

End point values	CB-03-01 solution, 2.5% BID	CB-03-01 solution, 5% BID	CB-03-01 solution 7.5% BID	CB-03-01 solution, 7.5% QD/vehicle solution QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	74	66	68	66
Units: Score				
Greatly decreased (-3)	0	1	1	1
Moderately decreased (-2)	3	4	5	2
Slightly decreased (-1)	4	8	6	4
No change (0)	22	13	14	22
Slightly increased (1)	23	17	20	21
Moderately increased (2)	17	18	20	12

Greatly increased (3)	5	4	2	4

End point values	Vehicle solution BID			
Subject group type	Reporting group			
Number of subjects analysed	70			
Units: Score				
Greatly decreased (-3)	1			
Moderately decreased (-2)	5			
Slightly decreased (-1)	9			
No change (0)	20			
Slightly increased (1)	17			
Moderately increased (2)	15			
Greatly increased (3)	3			

Statistical analyses

Statistical analysis title	Hair Growth Assesment (HGA) at Month 12

Statistical analysis description:

The frequency distribution of HGA score at Month 12 was evaluated using CMH mean score test stratified by analysis center using modified ridit score for between-group comparisons.
Pairwise comparisons between active treatment groups and vehicle were evaluated. If the table were sparse, Fisher's Exact test might have been used or categories might have been collapsed for analysis.

Comparison groups	CB-03-01 solution, 2.5% BID v CB-03-01 solution, 5% BID v CB-03-01 solution 7.5% BID v CB-03-01 solution, 7.5% QD/vehicle solution QD v Vehicle solution BID
Number of subjects included in analysis	344
Analysis specification	Pre-specified
Analysis type	other
P-value	≤ 0.05 [1]
Method	Cochran-Mantel-Haenszel

Notes:

[1] - Even if the p-value of the comparison vs vehicle was ≥ 0.2927, positive HGA scores 1 to 3 were reported in a higher share of subjects in all 4 active treatments groups when compared to the vehicle BID group (56.1% to 61.8% vs 50%) at month 12.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Information on the medical condition of subjects should have begun following the subject's written informed consent to participate in the study until the date of the final study visit.

Adverse event reporting additional description:

Treatment-emergent AEs (TEAEs) are AEs collected from the date of the first dose of IMP until the date of the final study visit.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21

Reporting groups

Reporting group title	CB-03-01 solution, 2.5% BID

Reporting group description:

CB-03-01 solution, 2.5% BID (twice a day)

Reporting group title	CB-03-01 solution, 5% BID

Reporting group description:

CB-03-01 solution, 5% BID (twice a day)

Reporting group title	CB-03-01 solution 7.5% BID

Reporting group description:

CB-03-01 solution 7.5% BID (twice a day)

Reporting group title	CB-03-01 solution, 7.5% QD/vehicle solution QD

Reporting group description:

CB-03-01 solution, 7.5% QD (once per day) and vehicle solution QD (once per day)

Reporting group title	Vehicle solution BID

Reporting group description:

Vehicle solution BID (twice a day)

Serious adverse events	CB-03-01 solution, 2.5% BID	CB-03-01 solution, 5% BID	CB-03-01 solution 7.5% BID
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 82 (2.44%)	2 / 78 (2.56%)	0 / 82 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Sinonasal papilloma	Additional description: This subject experienced a moderate recurrent inverted papilloma right paranasal sinus, about 4 months after first dose of IMP. The subject was hospitalized for a surgery to excise the papilloma.		
subjects affected / exposed	0 / 82 (0.00%)	0 / 78 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
B-cell lymphoma	Additional description: This subject experienced a severe B-cell lymphoma, about 4 months after first dose of IMP.		

subjects affected / exposed	0 / 82 (0.00%)	1 / 78 (1.28%)	0 / 82 (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
Renal neoplasm	Additional description: This subject experienced a moderate renal tumor about 10 months after first dose of IMP and was hospitalized for excision of the renal tumor.		
subjects affected / exposed	1 / 82 (1.22%)	0 / 78 (0.00%)	0 / 82 (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
Squamous cell carcinoma of the oral cavity	Additional description: This subject experienced a squamous cell carcinoma of the oral cavity and an oropharyngeal neoplasm about 8 months after first IMP dose.		
subjects affected / exposed	0 / 82 (0.00%)	0 / 78 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Dislocation of vertebra	Additional description: This subject experienced a moderate dislocation of cervical vertebra due to a motorcycle accident, about 6 months after first dose of IMP.		
subjects affected / exposed	0 / 82 (0.00%)	0 / 78 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendon rupture			
subjects affected / exposed	0 / 82 (0.00%)	1 / 78 (1.28%)	0 / 82 (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
Limb crushing injury	Additional description: This subject experienced a moderate crush injury of the right foot due to an accident about 13 months after first dose of IMP.		
subjects affected / exposed	0 / 82 (0.00%)	0 / 78 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Peripheral venous disease	Additional description: This subject experienced a moderate chronic venous insufficiency of the right leg about 5 months after first dose of IMP and was hospitalized from for phleboplasty.		
subjects affected / exposed	0 / 82 (0.00%)	0 / 78 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Appendicitis	Additional description: This subject experienced a severe appendicitis 12 months after first dose of IMP and was hospitalized on the same day for an		

	appendectomy.		
subjects affected / exposed	0 / 82 (0.00%)	0 / 78 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colon cancer	Additional description: This subject experienced a severe sigma carcinoma almost 10 months after first dose of IMP and was hospitalized for a sigma carcinoma section.		
subjects affected / exposed	0 / 82 (0.00%)	0 / 78 (0.00%)	0 / 82 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Emphysema	Additional description: This subject experienced a moderate pulmonary emphysema about 6 months after first dose of IMP. He was hospitalized due to this event for laboratory test controls.		
subjects affected / exposed	1 / 82 (1.22%)	0 / 78 (0.00%)	0 / 82 (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	CB-03-01 solution, 7.5% QD/vehicle solution QD	Vehicle solution BID	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 80 (2.50%)	5 / 82 (6.10%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Sinonasal papilloma	Additional description: This subject experienced a moderate recurrent inverted papilloma right paranasal sinus, about 4 months after first dose of IMP. The subject was hospitalized for a surgery to excise the papilloma.		
subjects affected / exposed	0 / 80 (0.00%)	1 / 82 (1.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
B-cell lymphoma	Additional description: This subject experienced a severe B-cell lymphoma, about 4 months after first dose of IMP.		
subjects affected / exposed	0 / 80 (0.00%)	0 / 82 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal neoplasm	Additional description: This subject experienced a moderate renal tumor about 10 months after first dose of IMP and was hospitalized for excision of the renal tumor.		

subjects affected / exposed	0 / 80 (0.00%)	0 / 82 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of the oral cavity	Additional description: This subject experienced a squamous cell carcinoma of the oral cavity and an oropharyngeal neoplasm about 8 months after first IMP dose.		
subjects affected / exposed	0 / 80 (0.00%)	1 / 82 (1.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Dislocation of vertebra	Additional description: This subject experienced a moderate dislocation of cervical vertebra due to a motorcycle accident, about 6 months after first dose of IMP.		
subjects affected / exposed	1 / 80 (1.25%)	0 / 82 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon rupture			
subjects affected / exposed	0 / 80 (0.00%)	0 / 82 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Limb crushing injury	Additional description: This subject experienced a moderate crush injury of the right foot due to an accident about 13 months after first dose of IMP.		
subjects affected / exposed	0 / 80 (0.00%)	1 / 82 (1.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Peripheral venous disease	Additional description: This subject experienced a moderate chronic venous insufficiency of the right leg about 5 months after first dose of IMP and was hospitalized from for phleboplasty.		
subjects affected / exposed	0 / 80 (0.00%)	1 / 82 (1.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Appendicitis	Additional description: This subject experienced a severe appendicitis 12 months after first dose of IMP and was hospitalized on the same day for an appendectomy.		
subjects affected / exposed	1 / 80 (1.25%)	0 / 82 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon cancer	Additional description: This subject experienced a severe sigma carcinoma almost 10 months after first dose of IMP and was hospitalized for a sigma		

	carcinoma section.		
subjects affected / exposed	0 / 80 (0.00%)	1 / 82 (1.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Emphysema	Additional description: This subject experienced a moderate pulmonary emphysema about 6 months after first dose of IMP. He was hospitalized due to this event for laboratory test controls.		
subjects affected / exposed	0 / 80 (0.00%)	0 / 82 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	CB-03-01 solution, 2.5% BID	CB-03-01 solution, 5% BID	CB-03-01 solution 7.5% BID
Total subjects affected by non-serious adverse events			
subjects affected / exposed	40 / 82 (48.78%)	39 / 78 (50.00%)	35 / 82 (42.68%)
Investigations			
Blood triglycerides increased			
subjects affected / exposed	5 / 82 (6.10%)	6 / 78 (7.69%)	7 / 82 (8.54%)
occurrences (all)	5	6	7
Alanine aminotransferase increased			
subjects affected / exposed	2 / 82 (2.44%)	1 / 78 (1.28%)	0 / 82 (0.00%)
occurrences (all)	2	1	0
Nervous system disorders			
Headache			
subjects affected / exposed	5 / 82 (6.10%)	6 / 78 (7.69%)	10 / 82 (12.20%)
occurrences (all)	6	6	13
General disorders and administration site conditions			
Application site pruritus			
subjects affected / exposed	5 / 82 (6.10%)	3 / 78 (3.85%)	2 / 82 (2.44%)
occurrences (all)	5	3	2
Application site dermatitis			
subjects affected / exposed	1 / 82 (1.22%)	3 / 78 (3.85%)	0 / 82 (0.00%)
occurrences (all)	2	3	0
Respiratory, thoracic and mediastinal disorders			

Nasopharyngitis			
subjects affected / exposed	22 / 82 (26.83%)	20 / 78 (25.64%)	16 / 82 (19.51%)
occurrences (all)	35	26	23

Non-serious adverse events	CB-03-01 solution, 7.5% QD/vehicle solution QD	Vehicle solution BID	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	43 / 80 (53.75%)	53 / 82 (64.63%)	
Investigations			
Blood triglycerides increased			
subjects affected / exposed	6 / 80 (7.50%)	9 / 82 (10.98%)	
occurrences (all)	6	9	
Alanine aminotransferase increased			
subjects affected / exposed	4 / 80 (5.00%)	0 / 82 (0.00%)	
occurrences (all)	4	0	
Nervous system disorders			
Headache			
subjects affected / exposed	8 / 80 (10.00%)	13 / 82 (15.85%)	
occurrences (all)	12	22	
General disorders and administration site conditions			
Application site pruritus			
subjects affected / exposed	2 / 80 (2.50%)	5 / 82 (6.10%)	
occurrences (all)	2	9	
Application site dermatitis			
subjects affected / exposed	4 / 80 (5.00%)	4 / 82 (4.88%)	
occurrences (all)	4	4	
Respiratory, thoracic and mediastinal disorders			
Nasopharyngitis			
subjects affected / exposed	19 / 80 (23.75%)	22 / 82 (26.83%)	
occurrences (all)	29	32	

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