



Clinical trial results:

An Open-label Extension Study of Levoketoconazole (2S,4R-ketoconazole) in the Treatment of Endogenous Cushing's Syndrome Summary

EudraCT number	2017-004647-20
Trial protocol	HU BG ES IT NL GR RO
Global end of trial date	30 December 2022

Results information

Result version number	v1 (current)
This version publication date	08 August 2025
First version publication date	08 August 2025

Trial information

Trial identification

Sponsor protocol code	COR-2017-OLE
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03621280
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Cortendo AB subsidiary of Xeris Biopharma Holdings
Sponsor organisation address	1375 West Fulton Street, Suite 1300, Chicago, Illinois, United States, 60607
Public contact	Clinical Trial Information, Valentina Conoscenti, +1 877-937-4737, clinicaltrials@xerispharma.com
Scientific contact	Clinical Trial Information, Valentina Conoscenti, +1 877-937-4737, clinicaltrials@xerispharma.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	02 March 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 December 2022
Global end of trial reached?	Yes
Global end of trial date	30 December 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess long-term safety and efficacy durability of levoketoconazole as chronic treatment for endogenous Cushing's Syndrome (CS).

Protection of trial subjects:

The study was designed, conducted, and monitored in accordance with the ethical principles set forth in the Declaration of Helsinki and the Guideline for ICH GCP (ICH E6). It also complied with the obligations and requirements of clinical investigators and all other requirements listed in 21 Code of Federal Regulations (CFR) 312. The Investigators conducted all aspects of this study in accordance with all national, state, and local laws of the pertinent regulatory authorities as well as the study procedures provided by Cortendo AB.

Background therapy:

There were no required or specified background therapies for this study.

Evidence for comparator:

The study was an open-label extension where all participants received levoketoconazole.

Actual start date of recruitment	07 January 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	Netherlands: 4
Country: Number of subjects enrolled	Poland: 2
Country: Number of subjects enrolled	Romania: 3
Country: Number of subjects enrolled	Spain: 2
Country: Number of subjects enrolled	Bulgaria: 9
Country: Number of subjects enrolled	France: 2
Country: Number of subjects enrolled	Greece: 5
Country: Number of subjects enrolled	Hungary: 2
Country: Number of subjects enrolled	Italy: 6
Country: Number of subjects enrolled	United States: 10
Country: Number of subjects enrolled	Israel: 6
Worldwide total number of subjects	51
EEA total number of subjects	35

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)	47
From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted in the United States, Israel, and Europe. Participants were recruited starting on 07Jan2019 through 03Dec2020 based on prior participation in COR-2012-01 and/or COR-2017-01. Participant eligibility was assessed prior to enrollment. 52 potential participants were screened and 51 participants were enrolled.

Pre-assignment

Screening details:

The study was a long-term open-label extension study of levoketoconazole in participants with endogenous Cushing's Syndrome who had completed one or both parent studies (COR-2012-01 and/or COR-2017-01) or participated in one of the parent studies and met specified inclusion criteria.

Period 1

Period 1 title	Treatment (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Levoketoconazole
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Arm description:

Establishment and treatment with a therapeutic dose of levoketoconazole (up to a dose of 1200 mg daily) based on normalization of mean urinary free cortisol (mUFC).

Arm type	Experimental
Investigational medicinal product name	Levoketoconazole
Investigational medicinal product code	COR-003
Other name	Recorlev
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

A single strength levoketoconazole tablet, 150 mg, was provided for oral administration. Individualized dosing for participants was established with dosing administered once or twice daily to achieve one of the following total daily doses: 150 mg, 300 mg, 450 mg, 600 mg, 750 mg, 900 mg, 1050 mg, 1200 mg.

Number of subjects in period 1	Levoketoconazole
Started	51
Completed	24
Not completed	27
Adverse event, serious fatal	3
Consent withdrawn by subject	6
Physician decision	5
Adverse event, non-fatal	11
Lack of efficacy	2

Baseline characteristics

Reporting groups

Reporting group title	Levoketoconazole
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Reporting group description:

Establishment and treatment with a therapeutic dose of levoketoconazole (up to a dose of 1200 mg daily) based on normalization of mean urinary free cortisol (mUFC).

Reporting group values	Levoketoconazole	Total	
Number of subjects	51	51	
Age categorical			
Units: Subjects			
Adults (18-64 years)	47	47	
From 65-84 years	4	4	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	44.1		
standard deviation	± 11.23	-	
Gender categorical			
Units: Subjects			
Female	40	40	
Male	11	11	
RACE			
Units: Subjects			
American Indian or Alaska Native	1	1	
Asian	0	0	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	3	3	
White	46	46	
More than one race	0	0	
Unknown or Not Reported	1	1	
Ethnicity			
Units: Subjects			
Hispanic or Latino	4	4	
Not Hispanic or Latino	47	47	
Unknown or Not Reported	0	0	
Receiving Anti-Diabetic Medication at COR-2017-OLE Baseline			
Units: Subjects			
Number of Participants	16	16	
Number of Participants Not Receiving	35	35	
Receiving Anti-Hypertensive Medication at COR-2017-OLE Baseline			
Units: Subjects			
Number of Participants	33	33	
Number of Participants Not Receiving	18	18	
Receiving Cholesterol-Reducing			

Medication at COR-2017-OLE Baseline Units: Subjects			
Number of Participants	8	8	
Number of Participants NOT Receiving	43	43	
Weight at COR-2017-OLE Baseline Units: kg arithmetic mean standard deviation	80.15 ± 18.994	-	
BMI at COR-2017-OLE Baseline Units: kg/m ² arithmetic mean standard deviation	29.57 ± 7.064	-	

End points

End points reporting groups

Reporting group title	Levoketoconazole
Reporting group description: Establishment and treatment with a therapeutic dose of levoketoconazole (up to a dose of 1200 mg daily) based on normalization of mean urinary free cortisol (mUFC).	
Subject analysis set title	Original Baseline
Subject analysis set type	Intention-to-treat
Subject analysis set description: The Original Baseline is the baseline value of mUFC relative to the ULN for the very first parent study (COR-2012-01 or COR-2017-01) that the participant was enrolled into.	
Subject analysis set title	OLE Baseline
Subject analysis set type	Sub-group analysis
Subject analysis set description: The OLE Baseline is the data from the participants that had an evaluable baseline mUFC at the start of COR-2017-OLE.	
Subject analysis set title	Month 6
Subject analysis set type	Sub-group analysis
Subject analysis set description: Month 6 is the data from participants that had an evaluable mUFC at the Month 6 analysis timepoint in COR-2017-OLE.	
Subject analysis set title	Month 12
Subject analysis set type	Sub-group analysis
Subject analysis set description: Month 12 is the data from participants that had an evaluable mUFC at the Month 12 analysis timepoint in COR-2017-OLE.	
Subject analysis set title	Month 18
Subject analysis set type	Sub-group analysis
Subject analysis set description: Month 18 is the data from participants that had an evaluable mUFC at the Month 18 analysis timepoint in COR-2017-OLE.	
Subject analysis set title	Month 24
Subject analysis set type	Sub-group analysis
Subject analysis set description: Month 24 is the data from participants that had an evaluable mUFC at the Month 24 analysis timepoint in COR-2017-OLE.	
Subject analysis set title	Month 30
Subject analysis set type	Sub-group analysis
Subject analysis set description: Month 30 is the data from participants that had an evaluable mUFC at the Month 30 analysis timepoint in COR-2017-OLE.	
Subject analysis set title	Month 36
Subject analysis set type	Sub-group analysis
Subject analysis set description: Month 36 is the data from participants that had an evaluable mUFC at the Month 36 analysis timepoint in COR-2017-OLE.	
Primary: Proportion of Participants with Mean Urinary Free Cortisol (mUFC) Categorization Based on Upper Limit of Normal (ULN)	
End point title	Proportion of Participants with Mean Urinary Free Cortisol (mUFC) Categorization Based on Upper Limit of Normal (ULN) ^[1]

End point description:

Proportions of participants with mUFC: 1) Less or equal to the ULN of the reference range, 2) Above the ULN to 1.5x the ULN, and 3) Above 1.5x the ULN.

End point type	Primary
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End point timeframe:

From parent study Baseline to final study visit or up to a maximum of 3 years, whichever comes first.

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The key exploratory endpoint (identified as the primary endpoint for this study) was an mUFC categorization based on ULN at specified visits. At each visit the number of subjects in the following categories were summarized for mUFC: 1) mUFC less than or equal to the ULN, 2) mUFC above the ULN to 1.5x ULN, and 3) mUFC above 1.5x ULN. No formal analysis was performed.

End point values	Original Baseline	OLE Baseline	Month 6	Month 12
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	51	50	40	37
Units: Number of Participants				
Less than or equal to ULN	0	26	20	15
Above ULN to 1.5x ULN	1	12	10	11
Above 1.5x ULN	50	12	10	11

End point values	Month 18	Month 24	Month 30	Month 36
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	28	29	24	13
Units: Number of Participants				
Less than or equal to ULN	16	18	15	7
Above ULN to 1.5x ULN	6	5	3	3
Above 1.5x ULN	6	6	6	3

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 3 years; from start of treatment through end of study.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	21.1
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Reporting groups

Reporting group title	All participants
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Reporting group description: -

Serious adverse events	All participants		
Total subjects affected by serious adverse events			
subjects affected / exposed	20 / 51 (39.22%)		
number of deaths (all causes)	3		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasm progression			
subjects affected / exposed	1 / 51 (1.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Aortic dissection			
subjects affected / exposed	1 / 51 (1.96%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Essential hypertension			
subjects affected / exposed	1 / 51 (1.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Pituitary tumour removal			
subjects affected / exposed	1 / 51 (1.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	1 / 51 (1.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dyspnoea			
subjects affected / exposed	1 / 51 (1.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Haemothorax			
subjects affected / exposed	1 / 51 (1.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pharyngeal haemorrhage			
subjects affected / exposed	1 / 51 (1.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary embolism			
subjects affected / exposed	1 / 51 (1.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Major depression			
subjects affected / exposed	1 / 51 (1.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Femoral neck fracture			
subjects affected / exposed	1 / 51 (1.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Angina unstable			

subjects affected / exposed	1 / 51 (1.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardio-respiratory arrest			
subjects affected / exposed	1 / 51 (1.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Pericardial effusion			
subjects affected / exposed	1 / 51 (1.96%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Presyncope			
subjects affected / exposed	1 / 51 (1.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
Ear canal stenosis			
subjects affected / exposed	1 / 51 (1.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	1 / 51 (1.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	1 / 51 (1.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypertansaminaemia			

subjects affected / exposed	1 / 51 (1.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	3 / 51 (5.88%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	1 / 51 (1.96%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hyperadrenocorticism			
subjects affected / exposed	1 / 51 (1.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	1 / 51 (1.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Corona virus infection			
subjects affected / exposed	3 / 51 (5.88%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 2		
Cellulitis			
subjects affected / exposed	1 / 51 (1.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Mediastinitis			

subjects affected / exposed	1 / 51 (1.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	1 / 51 (1.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Septic shock			
subjects affected / exposed	1 / 51 (1.96%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	All participants		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	48 / 51 (94.12%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	14 / 51 (27.45%)		
occurrences (all)	20		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	10 / 51 (19.61%)		
occurrences (all)	13		
Oedema peripheral			
subjects affected / exposed	4 / 51 (7.84%)		
occurrences (all)	5		
Pyrexia			
subjects affected / exposed	4 / 51 (7.84%)		
occurrences (all)	4		
Respiratory, thoracic and mediastinal disorders			
Cough			

subjects affected / exposed occurrences (all)	4 / 51 (7.84%) 5		
Psychiatric disorders Depression subjects affected / exposed occurrences (all)	5 / 51 (9.80%) 5		
Insomnia subjects affected / exposed occurrences (all)	4 / 51 (7.84%) 4		
Investigations Gamma glutamyltransferase increased subjects affected / exposed occurrences (all)	4 / 51 (7.84%) 5		
Alanine aminotransferase increased subjects affected / exposed occurrences (all)	3 / 51 (5.88%) 4		
Injury, poisoning and procedural complications Contusion subjects affected / exposed occurrences (all)	5 / 51 (9.80%) 5		
Cardiac disorders Palpitations subjects affected / exposed occurrences (all)	3 / 51 (5.88%) 4		
Nervous system disorders Headache subjects affected / exposed occurrences (all)	12 / 51 (23.53%) 21		
Dizziness subjects affected / exposed occurrences (all)	5 / 51 (9.80%) 5		
Sciatica subjects affected / exposed occurrences (all)	3 / 51 (5.88%) 4		
Blood and lymphatic system disorders			

Anaemia subjects affected / exposed occurrences (all)	3 / 51 (5.88%) 3		
Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all)	5 / 51 (9.80%) 5		
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Abdominal pain subjects affected / exposed occurrences (all) Abdominal pain upper subjects affected / exposed occurrences (all) Dyspepsia subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	17 / 51 (33.33%) 26 7 / 51 (13.73%) 11 3 / 51 (5.88%) 3 3 / 51 (5.88%) 4 3 / 51 (5.88%) 3 3 / 51 (5.88%) 6		
Skin and subcutaneous tissue disorders Dry skin subjects affected / exposed occurrences (all) Rash subjects affected / exposed occurrences (all) Alopecia subjects affected / exposed occurrences (all) Pruritis	6 / 51 (11.76%) 8 5 / 51 (9.80%) 6 3 / 51 (5.88%) 3		

subjects affected / exposed occurrences (all)	3 / 51 (5.88%) 4		
Endocrine disorders Adrenal insufficiency subjects affected / exposed occurrences (all)	5 / 51 (9.80%) 7		
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all) Arthralgia subjects affected / exposed occurrences (all) Muscle spasms subjects affected / exposed occurrences (all) Myalgia subjects affected / exposed occurrences (all) Neck pain subjects affected / exposed occurrences (all) Pain in extremity subjects affected / exposed occurrences (all)	7 / 51 (13.73%) 8 5 / 51 (9.80%) 7 3 / 51 (5.88%) 3 3 / 51 (5.88%) 3 3 / 51 (5.88%) 3		
Infections and infestations Corona virus infection subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all)	8 / 51 (15.69%) 8 5 / 51 (9.80%) 8 3 / 51 (5.88%) 3		
Metabolism and nutrition disorders			

Hypokalaemia			
subjects affected / exposed	12 / 51 (23.53%)		
occurrences (all)	15		
Decreased appetite			
subjects affected / exposed	3 / 51 (5.88%)		
occurrences (all)	4		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 July 2018	Key changes included the removal of the Data Monitoring Committee requirement for the study, updated inclusion of participants who completed COR-2012-01 or COR-2017-01 but had a break in therapy (this included adding information about the washout periods for drugs taken for Cushing's Syndrome and updating the timing of screening and baseline assessments for these participants), updating the language for the management of QTc interval prolongation.
23 September 2019	Key changes to the protocol included the addition of information to allow the enrollment of participants from COR-2017-01 that were enrolled in the dose titration phase of that study at the time entry into it's randomized-withdrawal phase was closed, additional clarification was also included for participants that had a gap in treatment prior to participating in COR-2017-OLE, and inclusion of an allowance (with Medical Monitor agreement) for a break in therapy while participating in the study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The protocol defined all efficacy endpoints as exploratory; however, the endpoint presented in this summary of results was the endpoint identified as the key exploratory endpoint.

Notes: