Clinical trial results:
A Phase II, randomized, open–label study to evaluate the efficacy and tolerability of treatment with vafidemstat in combination with standard of care treatment to prevent Acute Respiratory Distress Syndrome (ARDS) in adult severely ill patients with COVID-19.

Summary

EudraCT number	2020-001618-39
Trial protocol	ES
Global end of trial date	31 March 2021

Results information

Result version number	v1 (current)
This version publication date	20 April 2023
First version publication date	20 April 2023

Trial information

Trial identification

Sponsor protocol code	CL08-ORY-2001_COVID-19

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Oryzon Genomics S. A.
Sponsor organisation address	Carrer de Sant Ferran, 74, CORNELLA DE LLOBREGAT, Spain, 08940
Public contact	Douglas V. Faller, Chief Medical Officer, Oryzon Genomics S. A., 34 93 515 1313, dfaller@oryzon.com
Scientific contact	Douglas V. Faller, Chief Medical Officer, Oryzon Genomics S. A., 34 93 515 1313, dfaller@oryzon.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	12 January 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	31 March 2021
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To investigate the efficacy of vafidemstat, in combination with applicable standard of care treatment to prevent Acute Respiratory Distress Syndrome (ARDS) in adult severely ill patients with CoVID-19.

Protection of trial subjects:

In accordance with European Union RGPD 2016/679 of 27 April, 2016 the data were processed in accordance with the specifications outlined by the local law to ensure that requirements regarding personal data protection are met. If an external organization processed data on behalf of Oryzon, a contractual procedure was signed between Oryzon and the external organization to ensure compliance with the above-mentioned legislation. If applicable, the participation of patients in this study was reported to the appropriate local data protection agencies, in accordance with European Union RGPD 2016/679 of 27 April 2016 and Country-specific guidelines and laws (Spanish Organic Law 3/2018 of 5 December).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 May 2020
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	Spain: 60
Worldwide total number of subjects	60
EEA total number of subjects	60

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)	39

From 65 to 84 years	21
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 7 sites in Spain. Sixty patients were assigned, 29 in the SoC + vafidemstat group and 31 in the SoC group.

Pre-assignment

Screening details:

This study did not have a screening period. Patients were randomized to the study treatment after confirmation of selection criteria by investigator. Eligible patients were randomly allocated to one of two treatment groups in a 1:1 ratio (SoC: SoC + vafidemstat) by a strict order of inclusion in the study and following a randomization list.

Period 1

Period 1 title	Study Overall (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	SoC + vafidemstat

Arm description:

Vafidemstat was administered daily for 5 days, while fasting, at a dose of 2.4 mg/day in addition to SoC.

Arm type	Experimental
Investigational medicinal product name	Vafidemstat
Investigational medicinal product code	ORY-2001
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Vafidemstat was administered daily for 5 days, at a dose of 2.4 mg/day.

Arm title	Standard of Care (SoC)

Arm description:

SoC referred to any standard treatment assigned by the participating hospital centers according to the current guidelines

Arm type	Hospital current guidelines

No investigational medicinal product assigned in this arm

Number of subjects in period 1	SoC + vafidemstat	Standard of Care (SoC)
Started	29	31
Completed	29	31

Baseline characteristics

Reporting groups	
Reporting group title	SoC + vafidemstat
Reporting group description:	
Vafidemstat was administered daily for 5 days, while fasting, at a dose of 2.4 mg/day in addition to SoC.	
Reporting group title	Standard of Care (SoC)
Reporting group description:	
SoC referred to any standard treatment assigned by the participating hospital centers according to the current guidelines	

Reporting group values	SoC + vafidemstat	Standard of Care (SoC)	Total
Number of subjects	29	31	60
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)			0
From 65-84 years			0
85 years and over			0
Age continuous Units: years			
arithmetic mean	58.48	56.48	
standard deviation	± 14.51	± 14.64	-
Gender categorical Units: Subjects			
Female	8	15	23
Male	21	16	37

Subject analysis sets	
Subject analysis set title	FAS
Subject analysis set type	Full analysis
Subject analysis set description:	
All randomized patients who received at least one dose of the study treatment and with available data at Day 5 visit. Data from these patients were analyzed following the treatment planned as per randomization list.	
Subject analysis set title	PPS
Subject analysis set type	Per protocol
Subject analysis set description:	
All randomized patients of the FAS who met the selection criteria and were deemed to have no major protocol violations. This was a subpopulation of the FAS. Data from these patients were analyzed following the real treatment received	
Subject analysis set title	SAF
Subject analysis set type	Safety analysis

Subject analysis set description:

All randomized patients who received at least one dose of the study treatment. Data from these patients were analyzed following the real treatment received. The SAF population was used to analyze the safety and tolerability data.

Reporting group values	FAS	PPS	SAF
Number of subjects	60	60	60
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous Units: years			
arithmetic mean	57.45	57.45	57.45
standard deviation	± 14.48	± 14.48	± 14.48
Gender categorical Units: Subjects			
Female	23	23	23
Male	37	37	37

End points

End points reporting groups

Reporting group title	SoC + vafidemstat
Reporting group description:	
Vafidemstat was administered daily for 5 days, while fasting, at a dose of 2.4 mg/day in addition to SoC.	
Reporting group title	Standard of Care (SoC)
Reporting group description:	
SoC referred to any standard treatment assigned by the participating hospital centers according to the current guidelines	
Subject analysis set title	FAS
Subject analysis set type	Full analysis
Subject analysis set description:	
All randomized patients who received at least one dose of the study treatment and with available data at Day 5 visit. Data from these patients were analyzed following the treatment planned as per randomization list.	
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Subject analysis set description:	
All randomized patients of the FAS who met the selection criteria and were deemed to have no major protocol violations. This was a subpopulation of the FAS. Data from these patients were analyzed following the real treatment received	
Subject analysis set title	SAF
Subject analysis set type	Safety analysis
Subject analysis set description:	
All randomized patients who received at least one dose of the study treatment. Data from these patients were analyzed following the real treatment received. The SAF population was used to analyze the safety and tolerability data.	

Primary: Reduction in the incidence of patients (%) requiring mechanical ventilation / referral to ICU

End point title	Reduction in the incidence of patients (%) requiring mechanical ventilation / referral to ICU[1]
End point description:	
Reduction in the incidence of patients (%) requiring mechanical ventilation and referral to ICU within the period from Day 1 (i.e.: first study drug administration) to Day 14. As all analysis sets include the same number of patients (60) no subject analysis set has been specified.	
End point type	Primary
End point timeframe:	
From Day 1 (i.e.: first study drug administration) to Day 14	

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 PPS, which matched the FAS, was considered the primary analysis population for efficacy.
For continuous variables: parametric (Student’s t-test) or non-parametric tests (Mann–Whitney) for comparisons between groups and parametric (paired Student’s t-test) or non-parametric test (Wilcoxon) for comparisons between visits.
For categorical variables: Chi-squared test or Fisher’s exact test for comparisons between groups.

End point values	SoC + vafidemstat	Standard of Care (SoC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	31		
Units: Subjects				
mechanical ventilation	0	0		
referral to ICU	2	2		

Statistical analyses

No statistical analyses for this end point

Primary: Decrease in global mortality and mortality associated to CoVID-19 pneumonias

End point title	Decrease in global mortality and mortality associated to CoVID-19 pneumonias[2]

End point description:

Decrease in global mortality and mortality associated to CoVID-19 pneumonias within the period from Day 1 (i.e.: first study drug administration) to Day 14. As all analysis sets include the same number of patients (60) no subject analysis set has been specified.

End point type	Primary

End point timeframe:

From Day 1 (i.e.: first study drug administration) to Day 14

Notes:

[2] - 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 PPS, which matched the FAS, was considered the primary analysis population for efficacy.
For continuous variables: parametric (Student's t-test) or non-parametric tests (Mann–Whitney) for comparisons between groups and parametric (paired Student's t-test) or non-parametric test (Wilcoxon) for comparisons between visits.
For categorical variables: Chi-squared test or Fisher's exact test for comparisons between groups.

End point values	SoC + vafidemstat	Standard of Care (SoC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	31		
Units: Subjects				
Global Mortality	0	1		
Mortality Associated with CoVID-19	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Reduction in the incidence of patients (%) requiring mechanical ventilation / referral to ICU

End point title	Reduction in the incidence of patients (%) requiring mechanical ventilation / referral to ICU

End point description:

Reduction in the incidence of patients (%) requiring mechanical ventilation and referral to ICU within the

period from Day 15 to Day 28. As all analysis sets include the same number of patients (60) no subject analysis set has been specified.

End point type	Secondary

End point timeframe:

From Day 15 to Day 28

End point values	SoC + vafidemstat	Standard of Care (SoC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	31		
Units: Subjects				
Invasive mechanical ventilation	0	0		
Referral to ICU	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Decrease in global mortality and mortality associated to CoVID-19 pneumonias

End point title	Decrease in global mortality and mortality associated to CoVID-19 pneumonias

End point description:

Decrease in global mortality and mortality associated to CoVID-19 pneumonias within the period from Day 15 to Day 28. As all analysis sets include the same number of patients (60) no subject analysis set has been specified.

End point type	Secondary

End point timeframe:

From Day 15 to Day 28

End point values	SoC + vafidemstat	Standard of Care (SoC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	31		
Units: Subjects				
Global Mortality	0	0		
Mortality Associated with CoVID-19	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Improvement in O2Sat

End point title	Improvement in O2Sat

End point description:

Improvement in O2Sat (%) at Day 5, Day 14 and Day 28. As all analysis sets include the same number of patients (60) no subject analysis set has been specified.

End point type	Secondary

End point timeframe:

Day 5, Day 14 and Day 28

End point values	SoC + vafidemstat	Standard of Care (SoC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	31		
Units: Subjects				
Not changed / not improved	3	11		
Improved during the first 5 days	23	17		
Improved between Day 6 to Day 14	3	3		
Improved between Day 15 to Day 28	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Decrease in supplemental O2 needed

End point title	Decrease in supplemental O2 needed

End point description:

Decrease in supplemental O2 needed at Day 5, Day 14 and Day 28. Patient with non-invasive MV During the study.

End point type	Secondary

End point timeframe:

Day 5, Day 14 and Day 28

End point values	SoC + vafidemstat	Standard of Care (SoC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	23		
Units: Subjects				
Not changed / not improved	2	3		
Improved during the first 5 days	8	14		
Improved between Day 6 to Day 14	8	6		
Improved between Day 15 to Day 28	2	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to development of ARDS or respiratory failure for CoVID-19

End point title	Time to development of ARDS or respiratory failure for CoVID-19

End point description:

Time to development of ARDS or respiratory failure for CoVID-19 requiring intubation and mechanical ventilation from Day 1 to Day 28. As all analysis sets include the same number of patients (60) no subject analysis set has been specified.
Event-free survival (EFS), defining event as: requiring invasive MV, referral to ICU, requiring rescue medication or death associated with CoVID-19 comorbidities

End point type	Secondary

End point timeframe:

From Day 1 to Day 28

End point values	SoC + vafidemstat	Standard of Care (SoC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	31		
Units: Subjects				
Event-free survival (EFS)	3	5		

Statistical analyses

No statistical analyses for this end point

Secondary: Patients Requiring Rescue Medication

End point title	Patients Requiring Rescue Medication

End point description:

Reduce in the incidence of patients (%) requiring rescue medication such as anti IL-6 or corticoids

End point type	Secondary

End point timeframe:

During the Study

End point values	SoC + vafidemstat	Standard of Care (SoC)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	31		
Units: Subjects				
Patients required rescue medication	2	4		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Study period	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups	
Reporting group title	SoC + vafidemstat
Reporting group description:	
Vafidemstat was administered daily for 5 days, while fasting, at a dose of 2.4 mg/day in addition to SoC.	
Reporting group title	Standard of Care (SoC)
Reporting group description:	
SoC referred to any standard treatment assigned by the participating hospital centers according to the current guidelines	

Serious adverse events	SoC + vafidemstat	Standard of Care (SoC)	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 29 (0.00%)	0 / 31 (0.00%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events	0	0	

Frequency threshold for reporting non-serious adverse events: 3 %

Non-serious adverse events	SoC + vafidemstat	Standard of Care (SoC)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 29 (27.59%)	3 / 31 (9.68%)	
Investigations			
Neutrophil count decreased			
subjects affected / exposed	1 / 29 (3.45%)	2 / 31 (6.45%)	
occurrences (all)	1	2	
Nervous system disorders			
Dizziness postural			
subjects affected / exposed	1 / 29 (3.45%)	0 / 31 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			

Diarrhoea			
subjects affected / exposed	1 / 29 (3.45%)	1 / 31 (3.23%)	
occurrences (all)	1	1	
Nausea			
subjects affected / exposed	1 / 29 (3.45%)	0 / 31 (0.00%)	
occurrences (all)	1	0	
Gingival bleeding			
subjects affected / exposed	1 / 29 (3.45%)	0 / 31 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Erection increased			
subjects affected / exposed	1 / 29 (3.45%)	0 / 31 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	1 / 29 (3.45%)	0 / 31 (0.00%)	
occurrences (all)	1	0	
Pulmonary thrombosis			
subjects affected / exposed	1 / 29 (3.45%)	0 / 31 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Oropharyngeal candidiasis			
subjects affected / exposed	1 / 29 (3.45%)	0 / 31 (0.00%)	
occurrences (all)	1	0	
Oral candidiasis			
subjects affected / exposed	0 / 29 (0.00%)	1 / 31 (3.23%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 April 2020	Modified inclusion criteria #2 and #5 New exclusion criteria #1
25 May 2020	New sample for CyTOF analysis
23 June 2020	Modified inclusion criteria #2 Classification about Standard of Care Treatment
29 September 2020	Modified inclusion criteria #2 and exclusion criteria #1
02 February 2021	Increase in sample size

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.

Limited sample size

Notes: