Clinical trial results:
Phase 3, Randomized, Placebo-Controlled, Efficacy and Safety Study of VERU-111 for the Treatment of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) in Patients at High Risk for Acute Respiratory Distress Syndrome (ARDS)

Summary

EudraCT number	2021-001194-24
Trial protocol	BG
Global end of trial date	06 July 2022

Results information

Result version number	v1 (current)
This version publication date	21 June 2023
First version publication date	21 June 2023
Summary attachment (see zip file)	V3011902 Synopsis (v3011902-synopsis_Redacted.pdf)

Trial information

Trial identification

Sponsor protocol code	V3011902

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04842747
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Veru Inc.
Sponsor organisation address	2916 North Miami Ave, Miami, United States, 33127
Public contact	Veru Clinical Trials Rodriguez, Veru Inc., 001 800-606-9382, veruclinicaltrials@verupharma.com
Scientific contact	Veru Clinical Trials Barnette, Veru Inc., 001 800-606-9382, veruclinicaltrials@verupharma.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 July 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 July 2022
Global end of trial reached?	Yes
Global end of trial date	06 July 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the efficacy of VERU-111 in the treatment of SARS-CoV-2 infection by assessing its effect on the proportion of subjects that die on study (up to Day 60).

Protection of trial subjects:

Each subject was consented prior to participating in the trial according to ICH GCP guidelines.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 May 2021
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Bulgaria: 48
Country: Number of subjects enrolled	Argentina: 3
Country: Number of subjects enrolled	Brazil: 78
Country: Number of subjects enrolled	Colombia: 1
Country: Number of subjects enrolled	Mexico: 3
Country: Number of subjects enrolled	United States: 71
Worldwide total number of subjects	204
EEA total number of subjects	48

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)	106

From 65 to 84 years	96
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

244 patients were recruited at 37 sites across 6 countries in accordance with ICH/GCP guidelines.

Pre-assignment

Screening details:

All patients were screened within three days of Day 1 / randomization. Total of 244 patients were screened. 40 patients screen failed.

Period 1

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

Blinding implementation details:

All study team members with the exception of an unblinded statistician and the IDMC committee members were blinded.

Arms

Are arms mutually exclusive?	Yes
Arm title	9mg of VERU-111 Oral daily

Arm description:

Subjects in the VERU-111 treatment groups will receive standard of care, plus oral daily VERU-111 9mg for 21 days or until released from hospital.

Arm type	Experimental
Investigational medicinal product name	VERU-111
Investigational medicinal product code	
Other name	Sabizabulin
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects in the VERU-111 treatment groups will receive oral daily VERU-111 9 mg for 21 days or until released from hospital, whichever comes first.

Arm title	Placebo Capsule once daily

Arm description:

Subjects in the Placebo treatment group received standard of care, plus a placebo capsule for 21 days or until released from hospital.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects in the Placebo treatment group received one placebo capsule for 21 days or until released from hospital, whichever came first.

Number of subjects in period 1	9mg of VERU-111 Oral daily	Placebo Capsule once daily
Started	134	70
Completed	125	66
Not completed	9	4
Consent withdrawn by subject	6	2
Physician decision	1	-
PT refused all care decision made to withdraw PT	1	-
Lost to follow-up	1	2

Baseline characteristics

Reporting groups

Reporting group title	9mg of VERU-111 Oral daily
Reporting group description:	
Subjects in the VERU-111 treatment groups will receive standard of care, plus oral daily VERU-111 9mg for 21 days or until released from hospital.	
Reporting group title	Placebo Capsule once daily
Reporting group description:	
Subjects in the Placebo treatment group received standard of care, plus a placebo capsule for 21 days or until released from hospital.	

Reporting group values	9mg of VERU-111 Oral daily	Placebo Capsule once daily	Total
Number of subjects	134	70	204
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	61.3	62.7	
standard deviation	± 14.14	± 13.9	-
Gender categorical			
Units: Subjects			
Female	44	26	70
Male	90	44	134

Subject analysis sets

Subject analysis set title	Safety Set
Subject analysis set type	Safety analysis
Subject analysis set description:	
Safety Set: All randomized patients who received at least 1 dose of study drug (sabizabulin or placebo).	
Subject analysis set title	ITT Set
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All randomized patients	

Reporting group values	Safety Set	ITT Set	
Number of subjects	199	204	
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	61.6	61.8	
standard deviation	± 14.08	± 14.04	
Gender categorical Units: Subjects			
Female	67	70	
Male	132	134	

End points

End points reporting groups

Reporting group title	9mg of VERU-111 Oral daily
Reporting group description:	
Subjects in the VERU-111 treatment groups will receive standard of care, plus oral daily VERU-111 9mg for 21 days or until released from hospital.	
Reporting group title	Placebo Capsule once daily
Reporting group description:	
Subjects in the Placebo treatment group received standard of care, plus a placebo capsule for 21 days or until released from hospital.	
Subject analysis set title	Safety Set
Subject analysis set type	Safety analysis
Subject analysis set description:	
Safety Set: All randomized patients who received at least 1 dose of study drug (sabizabulin or placebo).	
Subject analysis set title	ITT Set
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All randomized patients	

Primary: Efficacy of sabizabulin in the treatment of SARS-CoV-2 infection by assessing its effect on the proportion of patients who died on study.

End point title	Efficacy of sabizabulin in the treatment of SARS-CoV-2 infection by assessing its effect on the proportion of patients who died on study.
End point description:	
The primary endpoint for the study was the proportion of patients who died on study (up to Day 60). Responders were patients who were alive at Day 60. The number and percentage of deaths were summarized by treatment group. The primary analysis was performed on the ITT Set, regardless of rescue medication use, protocol violations or study drug discontinuation, consistent with the treatment policy strategy.	
End point type	Primary
End point timeframe:	
Day 60	

End point values	9mg of VERU-111 Oral daily	Placebo Capsule once daily	ITT Set	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	134	70	204	
Units: 52				
number (confidence interval 95%)	8.14 (3.23 to 14.75)	2.79 (1.16 to 5.36)	2.79 (1.37 to 5.6)	

Statistical analyses

Statistical analysis title	Efficacy Analyses
Statistical analysis description:	
All statistical tests will be performed using a two-tailed 5% overall significance level, unless otherwise	

stated. All comparisons between treatments will be reported with 95% confidence intervals for the difference.

Comparison groups	9mg of VERU-111 Oral daily v Placebo Capsule once daily
Number of subjects included in analysis	204
Analysis specification	Pre-specified
Analysis type	superiority
P-value	≤ 0.0452 [1]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Confidence interval	
level	95 %
sides	2-sided

Notes:

[1] - 2 sided P Value. 1-sided P-value ≤0.0226 in favor of sabizabulin (final analysis).

Adverse events

Adverse events information

Timeframe for reporting adverse events:

First drug administration thru Day 60.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	Safety Set

Reporting group description: -

Serious adverse events	Safety Set		
Total subjects affected by serious adverse events			
subjects affected / exposed	70 / 199 (35.18%)		
number of deaths (all causes)	48		
number of deaths resulting from adverse events			
Investigations			
Liver function test abnormal			
subjects affected / exposed	1 / 199 (0.50%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Endotracheal intubation complication			
subjects affected / exposed	1 / 199 (0.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Post procedural haemorrhage			
subjects affected / exposed	1 / 199 (0.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Arterial thrombosis			
subjects affected / exposed	1 / 199 (0.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Deep vein thrombosis				
subjects affected / exposed	1 / 199 (0.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hypotension				
subjects affected / exposed	1 / 199 (0.50%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Hypovolaemic shock				
subjects affected / exposed	1 / 199 (0.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Peripheral artery thrombosis				
subjects affected / exposed	1 / 199 (0.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Peripheral embolism				
subjects affected / exposed	1 / 199 (0.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Shock				
subjects affected / exposed	1 / 199 (0.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Cardiac disorders				
Atrial fibrillation				
subjects affected / exposed	1 / 199 (0.50%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Bradycardia				
subjects affected / exposed	2 / 199 (1.01%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Cardiac arrest				

subjects affected / exposed	3 / 199 (1.51%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 1			
Cardio-respiratory arrest				
subjects affected / exposed	3 / 199 (1.51%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	1 / 2			
Cardiovascular insufficiency				
subjects affected / exposed	1 / 199 (0.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Pulmonary valve incompetence				
subjects affected / exposed	1 / 199 (0.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Brain injury				
subjects affected / exposed	1 / 199 (0.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cerebrovascular accident				
subjects affected / exposed	2 / 199 (1.01%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Coma				
subjects affected / exposed	1 / 199 (0.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Polyneuropathy				
subjects affected / exposed	1 / 199 (0.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Seizure like phenomena				

subjects affected / exposed	1 / 199 (0.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Stroke in evolution			
subjects affected / exposed	1 / 199 (0.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Death			
subjects affected / exposed	1 / 199 (0.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Multiple organ dysfunction syndrome			
subjects affected / exposed	2 / 199 (1.01%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 2		
Procedural failure			
subjects affected / exposed	1 / 199 (0.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Mydriasis			
subjects affected / exposed	1 / 199 (0.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	1 / 199 (0.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ischaemic hepatitis			
subjects affected / exposed	1 / 199 (0.50%)		
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	8 / 199 (4.02%)		
occurrences causally related to treatment / all	2 / 8		
deaths causally related to treatment / all	2 / 5		
Dyspnoea			
subjects affected / exposed	2 / 199 (1.01%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Hypoxia			
subjects affected / exposed	5 / 199 (2.51%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 3		
Laryngeal stenosis			
subjects affected / exposed	1 / 199 (0.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Organising pneumonia			
subjects affected / exposed	1 / 199 (0.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumomediastinum			
subjects affected / exposed	1 / 199 (0.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumothorax			
subjects affected / exposed	7 / 199 (3.52%)		
occurrences causally related to treatment / all	0 / 7		
deaths causally related to treatment / all	0 / 0		
Pulmonary embolism			
subjects affected / exposed	6 / 199 (3.02%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 1		

Pulmonary haemorrhage				
subjects affected / exposed	1 / 199 (0.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiration abnormal				
subjects affected / exposed	1 / 199 (0.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory acidosis				
subjects affected / exposed	1 / 199 (0.50%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Respiratory failure				
subjects affected / exposed	27 / 199 (13.57%)			
occurrences causally related to treatment / all	2 / 28			
deaths causally related to treatment / all	2 / 9			
Psychiatric disorders				
Delirium				
subjects affected / exposed	1 / 199 (0.50%)			
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	12 / 199 (6.03%)			
occurrences causally related to treatment / all	0 / 12			
deaths causally related to treatment / all	0 / 0			
Renal failure				
subjects affected / exposed	1 / 199 (0.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Renal impairment				
subjects affected / exposed	1 / 199 (0.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Tubulointerstitial nephritis				
subjects affected / exposed	1 / 199 (0.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Acinetobacter infection				
subjects affected / exposed	1 / 199 (0.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Burkholderia cepacia complex infection				
subjects affected / exposed	1 / 199 (0.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
COVID-19				
subjects affected / exposed	7 / 199 (3.52%)			
occurrences causally related to treatment / all	0 / 7			
deaths causally related to treatment / all	0 / 5			
COVID-19 pneumonia				
subjects affected / exposed	1 / 199 (0.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Clostridium difficile colitis				
subjects affected / exposed	1 / 199 (0.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Device related infection				
subjects affected / exposed	1 / 199 (0.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Endocarditis staphylococcal				
subjects affected / exposed	1 / 199 (0.50%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			

Enterococcal sepsis				
subjects affected / exposed	1 / 199 (0.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infection				
subjects affected / exposed	1 / 199 (0.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	8 / 199 (4.02%)			
occurrences causally related to treatment / all	0 / 11			
deaths causally related to treatment / all	0 / 4			
Pneumonia acinetobacter				
subjects affected / exposed	1 / 199 (0.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia bacterial				
subjects affected / exposed	2 / 199 (1.01%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Pulmonary sepsis				
subjects affected / exposed	3 / 199 (1.51%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	6 / 199 (3.02%)			
occurrences causally related to treatment / all	0 / 7			
deaths causally related to treatment / all	0 / 1			
Septic shock				
subjects affected / exposed	7 / 199 (3.52%)			
occurrences causally related to treatment / all	0 / 7			
deaths causally related to treatment / all	0 / 3			
Severe acute respiratory syndrome				

subjects affected / exposed	2 / 199 (1.01%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 2		
Urinary tract infection fungal			
subjects affected / exposed	2 / 199 (1.01%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection bacterial			
subjects affected / exposed	2 / 199 (1.01%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Urosepsis			
subjects affected / exposed	1 / 199 (0.50%)		
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	Safety Set		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	136 / 199 (68.34%)		
Vascular disorders			
Hypotension			
subjects affected / exposed	13 / 199 (6.53%)		
occurrences (all)	17		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	11 / 199 (5.53%)		
occurrences (all)	11		
Bradycardia			
subjects affected / exposed	11 / 199 (5.53%)		
occurrences (all)	12		
Blood and lymphatic system disorders			
Anemia			

subjects affected / exposed occurrences (all)	10 / 199 (5.03%) 10		
Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all)	 15 / 199 (7.54%) 19		
Respiratory, thoracic and mediastinal disorders Acute respiratory failure subjects affected / exposed occurrences (all) Hypoxia subjects affected / exposed occurrences (all) Pneumothorax subjects affected / exposed occurrences (all) Respiratory failure subjects affected / exposed occurrences (all)	 10 / 199 (5.03%) 10 7 / 199 (3.52%) 7 8 / 199 (4.02%) 8 27 / 199 (13.57%) 28		
Psychiatric disorders Anxiety subjects affected / exposed occurrences (all) Delirium subjects affected / exposed occurrences (all)	 8 / 199 (4.02%) 9 9 / 199 (4.52%) 9		
Renal and urinary disorders Acute kidney injury subjects affected / exposed occurrences (all)	 19 / 199 (9.55%) 19		
Infections and infestations Pneumonia subjects affected / exposed occurrences (all) Septic shock	 17 / 199 (8.54%) 24 		

subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all)	7 / 199 (3.52%) 7 9 / 199 (4.52%) 9		
Metabolism and nutrition disorders Hyperkalemia subjects affected / exposed occurrences (all) Hypernatremia subjects affected / exposed occurrences (all) Hypokalemia subjects affected / exposed occurrences (all)	 12 / 199 (6.03%) 13 10 / 199 (5.03%) 10 11 / 199 (5.53%) 14		

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