Clinical trial results:
A randomized, double blind, placebo-controlled, phase 2 clinical trial to investigate the efficacy and safety of 2 doses of NuSepin® intravenous infusion in Covid-19 pneumonia patients

Summary

EudraCT number	2020-003107-34
Trial protocol	RO
Global end of trial date	05 April 2021

Results information

Result version number	v1 (current)
This version publication date	26 August 2022
First version publication date	26 August 2022

Trial information

Trial identification

Sponsor protocol code	SHAPERON001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04565379
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Shaperon Inc.
Sponsor organisation address	174-10 Jagok-ro, Gangnam-gu, Seoul, Korea, Republic of,
Public contact	Clinical Trial Desk, Shaperon Inc, ctdesk@shaperon.com
Scientific contact	Clinical Trial Desk, Shaperon Inc, ctdesk@shaperon.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	25 June 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	05 April 2021
Global end of trial reached?	Yes
Global end of trial date	05 April 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Evaluation of efficacy of NuSepin® intravenous infusion in patients with SARS-CoV-2 infection

Protection of trial subjects:

Subject safety, well-being and data integrity was protected by compliance with the study Protocol, GCP and local regulations and guidelines throughout the study

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	29 July 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	Romania: 64
Worldwide total number of subjects	64
EEA total number of subjects	64

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)	44
From 65 to 84 years	20
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Eligible subjects were undergone screening tests and procedures after signature of Patient Information Sheet and the Informed Consent Form. The procedures were include collecting demographic information, medical history, previous and concomitant medication, measurement of vital signs, a physical examination, routine laboratory exam, etc.

Period 1

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

Blinding implementation details:

Dedicated unblinded site staff (pharmacists) were assigned at each site to prepare the IP infusions. All other team members, and all subjects, were blinded.

Arms

Are arms mutually exclusive?	Yes
Arm title	NuSepin 0.1 mg/kg

Arm description:

NuSepin powder dissolved and diluted for infusion at 0.1 mg/kg in 100 ml NaCl solution.

Arm type	Experimental
Investigational medicinal product name	NuSepin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

NuSepin powder dissolved and diluted for infusion at 0.1 mg/kg in 100 ml NaCl solution.

Arm title	NuSepin 0.2 mg/kg

Arm description:

NuSepin powder dissolved and diluted for infusion at 0.2 mg/kg in 100 ml NaCl solution.

Arm type	Experimental
Investigational medicinal product name	NuSepin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

NuSepin powder dissolved and diluted for infusion at 0.2 mg/kg in 100 ml NaCl solution.

Arm title	Placebo

Arm description:

Placebo infusion of standard 100 ml NaCl solution.

Arm type	Placebo

Investigational medicinal product name	Normal Saline
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

100 ml normal saline infusion as placebo

Number of subjects in period 1	NuSepin 0.1 mg/kg	NuSepin 0.2 mg/kg	Placebo
Started	22	22	20
Completed	18	21	18
Not completed	4	1	2
Consent withdrawn by subject	1	-	-
Adverse event, non-fatal	-	-	2
steroid treatment was started because of worsening	3	-	-
disease progression	-	1	-

Baseline characteristics

Reporting groups	
Reporting group title	NuSepin 0.1 mg/kg
Reporting group description:	
NuSepin powder dissolved and diluted for infusion at 0.1 mg/kg in 100 ml NaCl solution.	
Reporting group title	NuSepin 0.2 mg/kg
Reporting group description:	
NuSepin powder dissolved and diluted for infusion at 0.2 mg/kg in 100 ml NaCl solution.	
Reporting group title	Placebo
Reporting group description:	
Placebo infusion of standard 100 ml NaCl solution.	

Reporting group values	NuSepin 0.1 mg/kg	NuSepin 0.2 mg/kg	Placebo
Number of subjects	22	22	20
Age categorical Units: Subjects			
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	16	15	13
From 65-84 years	6	7	7
85 years and over	0	0	0
Age continuous Units: years			
median	62	59	63
inter-quartile range (Q1-Q3)	58 to 66	54 to 68	56 to 69
Gender categorical Units: Subjects			
Female	12	10	10
Male	10	12	10

Reporting group values	Total		
Number of subjects	64		
Age categorical Units: Subjects			
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)	44		
From 65-84 years	20		
85 years and over	0		
Age continuous Units: years			
median			

inter-quartile range (Q1-Q3)	-		

Gender categorical Units: Subjects			
Female	32		
Male	32		

Subject analysis sets	
Subject analysis set title	SAS
Subject analysis set type	Safety analysis
Subject analysis set description: All randomized patients	
Subject analysis set title	ITT
Subject analysis set type	Intention-to-treat
Subject analysis set description: All SAS patients receiving at least one dose of study medication and having at least one post-baseline efficacy measurement	
Subject analysis set title	mITT
Subject analysis set type	Modified intention-to-treat
Subject analysis set description: All ITT patients who had at baseline 6-category ordinal scale ≥3 - used only for the primary efficacy endpoint	
Subject analysis set title	PP
Subject analysis set type	Per protocol
Subject analysis set description: All patients completing the study without major protocol deviations	

Reporting group values	SAS	ITT	mITT
Number of subjects	64	64	61
Age categorical Units: Subjects			
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	44	44	42
From 65-84 years	20	20	19
85 years and over	0	0	0
Age continuous Units: years			
median	61	61	61
inter-quartile range (Q1-Q3)	57 to 67	57 to 67	57 to 67
Gender categorical Units: Subjects			
Female	32	32	30
Male	32	32	31

Reporting group values	PP		
Number of subjects	54		

Age categorical Units: Subjects			
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)	37		
From 65-84 years	17		
85 years and over	0		
Age continuous Units: years			
median	61		
inter-quartile range (Q1-Q3)	57 to 68		
Gender categorical Units: Subjects			
Female	26		
Male	28		

End points

End points reporting groups

Reporting group title	NuSepin 0.1 mg/kg
Reporting group description:	
NuSepin powder dissolved and diluted for infusion at 0.1 mg/kg in 100 ml NaCl solution.	
Reporting group title	NuSepin 0.2 mg/kg
Reporting group description:	
NuSepin powder dissolved and diluted for infusion at 0.2 mg/kg in 100 ml NaCl solution.	
Reporting group title	Placebo
Reporting group description:	
Placebo infusion of standard 100 ml NaCl solution.	
Subject analysis set title	SAS
Subject analysis set type	Safety analysis
Subject analysis set description:	
All randomized patients	
Subject analysis set title	ITT
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All SAS patients receiving at least one dose of study medication and having at least one post-baseline efficacy measurement	
Subject analysis set title	mITT
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
All ITT patients who had at baseline 6-category ordinal scale ≥3 - used only for the primary efficacy endpoint	
Subject analysis set title	PP
Subject analysis set type	Per protocol
Subject analysis set description:	
All patients completing the study without major protocol deviations	

Primary: Difference in Time to Clinical Improvement (TTCI) between the 2 treatment and the placebo group

End point title	Difference in Time to Clinical Improvement (TTCI) between the 2 treatment and the placebo group[1]
End point description:	
The primary endpoint parameter is time to clinical improvement (censored at Day 29), defined as the time (in days) from randomization of study treatment (NuSepin or placebo) until a decline of two categories on a six-category ordinal scale* of clinical status (1 = complete clinical remission; 6 = death) * Six-category ordinal scale: 6. Death; 5. ICU, requiring ECMO and/or IMV; 4. ICU/hospitalization, requiring NIV/ HFNC therapy; 3.Hospitalization, requiring supplemental oxygen (such as LFNC or facial mask); 2. Hospitalization, not requiring supplemental oxygen; 1. Complete clinical remission, i.e. fever, respiratory rate, oxygen saturation return to normal, and cough relief). Abbreviations: IMV= invasive mechanical ventilation; NIV=non-invasive mechanical ventilation; HFNC=High-flow nasal cannula; LFNC= Low-flow nasal cannula.	
End point type	Primary
End point timeframe:	
Up to 29 days	
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: Currently, there is an ongoing discussion for business partners about licensing out of this compound.	

Therefore, the results of endpoints are confidential and it is difficult to post them to open public source. Shaperon would be very much appreciated if EudraCT accepts the late posting.

Thank you

End point values	NuSepin 0.1 mg/kg	NuSepin 0.2 mg/kg	Placebo	ITT
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	22[2]	22[3]	20[4]	64
Units: Days	22	22	20	64

Notes:

[2] - Subjects with NuSepin 0.1 mg/kg treatment

[3] - Subjects with NuSepin 0.2 mg/kg treatment

[4] - Subjects with SOC (placebo) treatment

End point values	mITT	PP		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	61	54		
Units: Days	61	54		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

After the treatment start day (day1), the follow-up period starts and continues until Day 29, when the last study visit (EoS) will take place. If subjects are discharged within the visit window of EoS visit, they go through EoS procedures.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	Placebo
Reporting group description:	
Group for SOC treatments	
Reporting group title	NuSepin 0.1 mg/kg
Reporting group description:	
Group for SOC with NuSepin 0.1 mg/kg treatment	
Reporting group title	NuSepin 0.2 mg/kg
Reporting group description:	
Group for SOC with NuSepin 0.2 mg/kg treatment	

Serious adverse events	Placebo	NuSepin 0.1 mg/kg	NuSepin 0.2 mg/kg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 20 (0.00%)	0 / 22 (0.00%)	1 / 22 (4.55%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 20 (0.00%)	0 / 22 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Placebo	NuSepin 0.1 mg/kg	NuSepin 0.2 mg/kg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 20 (20.00%)	6 / 22 (27.27%)	5 / 22 (22.73%)
Investigations			

Alanine aminotransferase increased			
subjects affected / exposed	2 / 20 (10.00%)	0 / 22 (0.00%)	0 / 22 (0.00%)
occurrences (all)	2	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 20 (0.00%)	1 / 22 (4.55%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
C-reactive protein increased			
subjects affected / exposed	0 / 20 (0.00%)	1 / 22 (4.55%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 20 (0.00%)	2 / 22 (9.09%)	2 / 22 (9.09%)
occurrences (all)	0	2	2
Hepatic enzyme increased			
subjects affected / exposed	0 / 20 (0.00%)	2 / 22 (9.09%)	1 / 22 (4.55%)
occurrences (all)	0	2	1
Neutrophil count increased			
subjects affected / exposed	0 / 20 (0.00%)	1 / 22 (4.55%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 20 (0.00%)	1 / 22 (4.55%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Cardiac disorders			
Tachycardia			
subjects affected / exposed	3 / 20 (15.00%)	1 / 22 (4.55%)	0 / 22 (0.00%)
occurrences (all)	3	1	0
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 20 (10.00%)	0 / 22 (0.00%)	2 / 22 (9.09%)
occurrences (all)	2	0	2
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 20 (0.00%)	1 / 22 (4.55%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Leukocytosis			

subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	1 / 22 (4.55%) 1	0 / 22 (0.00%) 0
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 22 (0.00%) 0	1 / 22 (4.55%) 1
Hepatobiliary disorders Hepatic cytolysis subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 22 (0.00%) 0	2 / 22 (9.09%) 2
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	1 / 22 (4.55%) 1	0 / 22 (0.00%) 0
Metabolism and nutrition disorders Hypokalaemia subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 22 (0.00%) 0	1 / 22 (4.55%) 1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 February 2021	Inclusion criteria is added 1) Patients with NEWS2 score > 7 2)In order to be able to reach the primary endpoint, only subjects with clinical status 3 or higher (i.e.worse) should be considered for enrollment.

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 present study has several limitations because of limited sample size. Large-scale validation 19 study would increase the generalizability of our results.

Notes: