



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

| | | | |
|--|---------------------|---------------------|---------------------|
| 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: