



Clinical trial results:

A Double-blind, Randomised, Placebo-controlled, Phase 2b/3 Adaptive Clinical Trial Investigating the Efficacy and Safety of Selepressin as Treatment for Patients with Vasopressor-dependent Septic Shock

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2014-003973-41 |
| Trial protocol | BE NL FR DK |
| Global end of trial date | 26 February 2018 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 (current) |
| This version publication date | 08 March 2019 |
| First version publication date | 08 March 2019 |

Trial information

Trial identification

| | |
|-----------------------|--------|
| Sponsor protocol code | 000133 |
|-----------------------|--------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02508649 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Ferring Pharmaceuticals A/S |
| Sponsor organisation address | International PharmaScience Center, Kay Fiskers Plads 11, Copenhagen S, Denmark, 2300 |
| Public contact | Global Clinical Compliance, Ferring pharmaceuticals, DK0-Disclosure@ferring.com |
| Scientific contact | Global Clinical Compliance, Ferring pharmaceuticals, DK0-Disclosure@ferring.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 | 26 February 2018 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 03 October 2017 |
| Global end of trial reached? | Yes |
| Global end of trial date | 26 February 2018 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

To demonstrate superiority of selepressin plus standard care versus placebo plus standard care in the number of vasopressor- and mechanical ventilator-free days (with penalty for mortality) in subjects with vasopressor-dependent septic shock.

Protection of trial subjects:

The trial was performed in accordance with the Declaration of Helsinki and its amendments in force at the initiation of the trial, in compliance with the approved protocol and its amendments, Good Clinical Practice and applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

| | |
|---|--------------|
| Actual start date of recruitment | 31 July 2015 |
| 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: 21 |
| Country: Number of subjects enrolled | Belgium: 242 |
| Country: Number of subjects enrolled | Denmark: 213 |
| Country: Number of subjects enrolled | France: 335 |
| Country: Number of subjects enrolled | United States: 57 |
| Worldwide total number of subjects | 868 |
| EEA total number of subjects | 811 |

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) | 337 |
| From 65 to 84 years | 479 |
| 85 years and over | 52 |

Subject disposition

Recruitment

Recruitment details:

A total of 63 sites were authorised to recruit subjects for the trial between July 2015 and August 2017. Eleven of these sites did not recruit any subjects. The trial sites that randomised subjects to the trial were: 11 in Belgium, 5 in Denmark, 17 in France, 5 in the Netherlands, and 14 in the United States of America.

Pre-assignment

Screening details:

A total of 6377 subjects were screened, of which 868 subjects were randomised (585 subjects were allocated to selepressin [three doses] and 283 subjects were allocated to placebo). Up to four dosing regimens of selepressin were planned to be investigated in the trial. However, the highest dosing regimen was not used.

Period 1

| | |
|------------------------------|-------------------------|
| Period 1 title | Overall Trial Period |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Investigator, Subject |

Arms

| | |
|------------------------------|---------|
| Are arms mutually exclusive? | Yes |
| Arm title | Placebo |

Arm description:

Sterile 0.9% sodium chloride solution given as an infusion.

| | |
|--|-----------------------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Sterile 0.9% sodium chloride solution given as an infusion.

| | |
|------------------|---------------------------|
| Arm title | Selepressin 2.5 ng/kg/Min |
|------------------|---------------------------|

Arm description:

Starting dose: 1.7 ng/kg/min selepressin; Maximum dose: 2.5 ng/kg/min selepressin, given as an infusion.

| | |
|--|---------------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Selepressin 2.5 ng/kg/Min |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Starting dose: 1.7 ng/kg/min selepressin; Maximum dose: 2.5 ng/kg/min selepressin, given as an infusion.

| | |
|------------------|----------------------------|
| Arm title | Selepressin 3.75 ng/kg/Min |
|------------------|----------------------------|

Arm description:

Starting dose: 2.5 ng/kg/min selepressin; Maximum dose: 3.75 ng/kg/min selepressin, given as an infusion.

| | |
|--|---------------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Selepressin 3.75 ng/kg/Min |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Starting dose: 2.5 ng/kg/min selepressin; Maximum dose: 3.75 ng/kg/min selepressin, given as an infusion.

| | |
|------------------|----------------------------|
| Arm title | Selepressin 5.25 ng/kg/Min |
|------------------|----------------------------|

Arm description:

Starting dose: 3.5 ng/kg/min selepressin; Maximum dose: 5.25 ng/kg/min selepressin, given as an infusion.

| | |
|--|---------------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Selepressin 5.25 ng/kg/Min |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Starting dose: 3.5 ng/kg/min selepressin; Maximum dose: 5.25 ng/kg/min selepressin, given as an infusion.

| | |
|------------------|--------------------|
| Arm title | Selepressin Pooled |
|------------------|--------------------|

Arm description:

All selepressin arms pooled together and treated as a single arm.

| | |
|--|---------------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Selepressin Pooled |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

All selepressin arms pooled together and treated as a single arm.

| Number of subjects in period 1 | Placebo | Selepressin 2.5 ng/kg/Min | Selepressin 3.75 ng/kg/Min |
|---------------------------------------|---------|---------------------------|----------------------------|
| Started | 283 | 197 | 189 |
| Dosed | 266 | 191 | 177 |
| Completed | 265 | 184 | 174 |
| Not completed | 18 | 13 | 15 |
| Post randomisation screening failure | 12 | 4 | 9 |
| Physician decision | 1 | 2 | 1 |
| Consent withdrawn by subject | 4 | 6 | 5 |
| Lost to follow-up | 1 | 1 | - |

| | | |
|---------------------------------------|----------------------------|--------------------|
| Number of subjects in period 1 | Selepressin 5.25 ng/kg/Min | Selepressin Pooled |
|---------------------------------------|----------------------------|--------------------|

| | | |
|--------------------------------------|-----|-----|
| Started | 199 | 585 |
| Dosed | 194 | 562 |
| Completed | 189 | 547 |
| Not completed | 10 | 38 |
| Post randomisation screening failure | 3 | 16 |
| Physician decision | - | 3 |
| Consent withdrawn by subject | 6 | 17 |
| Lost to follow-up | 1 | 2 |

Period 2

| | |
|------------------------------|-------------------------|
| Period 2 title | Baseline Period |
| Is this the baseline period? | Yes ^[1] |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator |

Blinding implementation details:

This was a double-blind trial in which the subjects, the investigators and the other trial site staff, the clinical coordinating centres, the trial steering committee, the clinical trial team at Ferring and its representatives were blinded to the treatment assignment.

Arms

| | |
|------------------------------|---------|
| Are arms mutually exclusive? | No |
| Arm title | Placebo |

Arm description:

Sterile 0.9% sodium chloride solution given as an infusion.

| | |
|--|-----------------------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Sterile 0.9% sodium chloride solution given as an infusion.

| | |
|------------------|---------------------------|
| Arm title | Selepressin 2.5 ng/kg/Min |
|------------------|---------------------------|

Arm description:

Starting dose: 1.7 ng/kg/min selepressin; Maximum dose: 2.5 ng/kg/min selepressin, given as an infusion.

| | |
|--|---------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Selepressin 2.5 ng/kg/Min |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Starting dose: 1.7 ng/kg/min selepressin; Maximum dose: 2.5 ng/kg/min selepressin, given as an infusion.

| | |
|------------------|----------------------------|
| Arm title | Selepressin 3.75 ng/kg/Min |
|------------------|----------------------------|

Arm description:

Starting dose: 2.5 ng/kg/min selepressin; Maximum dose: 3.75 ng/kg/min selepressin, given as an infusion.

| | |
|--|---------------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Selepressin 3.75 ng/kg/Min |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Starting dose: 2.5 ng/kg/min selepressin; Maximum dose: 3.75 ng/kg/min selepressin, given as an infusion.

| | |
|------------------|----------------------------|
| Arm title | Selepressin 5.25 ng/kg/Min |
|------------------|----------------------------|

Arm description:

Starting dose: 3.5 ng/kg/min selepressin; Maximum dose: 5.25 ng/kg/min selepressin, given as an infusion.

| | |
|--|---------------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Selepressin 5.25 ng/kg/Min |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Starting dose: 3.5 ng/kg/min selepressin; Maximum dose: 5.25 ng/kg/min selepressin, given as an infusion.

| | |
|------------------|--------------------|
| Arm title | Selepressin Pooled |
|------------------|--------------------|

Arm description:

All selepressin arms pooled together and treated as a single arm.

| | |
|--|---------------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Selepressin Pooled |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

All selepressin arms pooled together and treated as a single arm.

Notes:

[1] - Period 1 is not the baseline period. It is expected that period 1 will be the baseline period.

Justification: Period 1 included all subjects that were enrolled in the trial whereas Period 2 included all subjects that were dosed in the trial. Baseline data, efficacy, and safety outcomes are presented for all the dosed subjects.

| Number of subjects in period 2 | Placebo | Selepressin 2.5 ng/kg/Min | Selepressin 3.75 ng/kg/Min |
|---------------------------------------|---------|---------------------------|----------------------------|
| Started | 266 | 191 | 177 |
| Completed | 263 | 184 | 172 |
| Not completed | 3 | 7 | 5 |
| Consent withdrawn by subject | 2 | 6 | 5 |
| Lost to follow-up | 1 | 1 | - |

| Number of subjects in period 2 | Selepressin 5.25 ng/kg/Min | Selepressin Pooled |
|---------------------------------------|----------------------------|--------------------|
| Started | 194 | 562 |

| | | |
|------------------------------|-----|-----|
| Completed | 187 | 543 |
| Not completed | 7 | 19 |
| Consent withdrawn by subject | 6 | 17 |
| Lost to follow-up | 1 | 2 |

Baseline characteristics

Reporting groups^[1]

| | |
|---|----------------------------|
| Reporting group title | Placebo |
| Reporting group description: Sterile 0.9% sodium chloride solution given as an infusion. | |
| Reporting group title | Selepressin 2.5 ng/kg/Min |
| Reporting group description: Starting dose: 1.7 ng/kg/min selepressin; Maximum dose: 2.5 ng/kg/min selepressin, given as an infusion. | |
| Reporting group title | Selepressin 3.75 ng/kg/Min |
| Reporting group description: Starting dose: 2.5 ng/kg/min selepressin; Maximum dose: 3.75 ng/kg/min selepressin, given as an infusion. | |
| Reporting group title | Selepressin 5.25 ng/kg/Min |
| Reporting group description: Starting dose: 3.5 ng/kg/min selepressin; Maximum dose: 5.25 ng/kg/min selepressin, given as an infusion. | |
| Reporting group title | Selepressin Pooled |
| Reporting group description: All selepressin arms pooled together and treated as a single arm. | |

Notes:

[1] - The number of subjects reported to be in the baseline period is not equal to the worldwide number of subjects enrolled in the trial. It is expected that these numbers will be the same.

Justification: Period 1 included all subjects that were enrolled in the trial whereas Period 2 included all subjects that were dosed in the trial. Baseline data, efficacy, and safety outcomes are presented for all the dosed subjects.

| Reporting group values | Placebo | Selepressin 2.5 ng/kg/Min | Selepressin 3.75 ng/kg/Min |
|---|---------|---------------------------|----------------------------|
| Number of subjects | 266 | 191 | 177 |
| 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 | | | |
| geometric mean | 65.7 | 66.0 | 67.2 |
| standard deviation | ± 14.56 | ± 12.76 | ± 13.13 |
| Gender categorical Units: Subjects | | | |
| Female | 121 | 80 | 70 |
| Male | 145 | 111 | 107 |

| | | | |
|---|-----|-----|-----|
| Ethnicity | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 4 | 3 | 1 |
| Not Hispanic or Latino | 262 | 188 | 176 |
| Unknown or Not Reported | 0 | 0 | 0 |
| Race | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 1 | 0 | 0 |
| Asian | 1 | 2 | 5 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |
| Black or African American | 4 | 3 | 11 |
| White | 260 | 186 | 161 |

| Reporting group values | Selepressin 5.25 ng/kg/Min | Selepressin Pooled | Total |
|---|-------------------------------|--------------------|-------|
| Number of subjects | 194 | 562 | 828 |
| 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 | | | |
| geometric mean | 66.8 | 66.6 | |
| standard deviation | ± 12.47 | ± 12.76 | - |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 70 | 220 | 341 |
| Male | 124 | 342 | 487 |
| Ethnicity | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 4 | 8 | 12 |
| Not Hispanic or Latino | 190 | 554 | 816 |
| Unknown or Not Reported | 0 | 0 | 0 |
| Race | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | 1 |
| Asian | 4 | 11 | 12 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |
| Black or African American | 7 | 21 | 25 |
| White | 183 | 530 | 790 |

End points

End points reporting groups

| | |
|---|----------------------------|
| Reporting group title | Placebo |
| Reporting group description: Sterile 0.9% sodium chloride solution given as an infusion. | |
| Reporting group title | Selepressin 2.5 ng/kg/Min |
| Reporting group description: Starting dose: 1.7 ng/kg/min selepressin; Maximum dose: 2.5 ng/kg/min selepressin, given as an infusion. | |
| Reporting group title | Selepressin 3.75 ng/kg/Min |
| Reporting group description: Starting dose: 2.5 ng/kg/min selepressin; Maximum dose: 3.75 ng/kg/min selepressin, given as an infusion. | |
| Reporting group title | Selepressin 5.25 ng/kg/Min |
| Reporting group description: Starting dose: 3.5 ng/kg/min selepressin; Maximum dose: 5.25 ng/kg/min selepressin, given as an infusion. | |
| Reporting group title | Selepressin Pooled |
| Reporting group description: All selepressin arms pooled together and treated as a single arm. | |
| Reporting group title | Placebo |
| Reporting group description: Sterile 0.9% sodium chloride solution given as an infusion. | |
| Reporting group title | Selepressin 2.5 ng/kg/Min |
| Reporting group description: Starting dose: 1.7 ng/kg/min selepressin; Maximum dose: 2.5 ng/kg/min selepressin, given as an infusion. | |
| Reporting group title | Selepressin 3.75 ng/kg/Min |
| Reporting group description: Starting dose: 2.5 ng/kg/min selepressin; Maximum dose: 3.75 ng/kg/min selepressin, given as an infusion. | |
| Reporting group title | Selepressin 5.25 ng/kg/Min |
| Reporting group description: Starting dose: 3.5 ng/kg/min selepressin; Maximum dose: 5.25 ng/kg/min selepressin, given as an infusion. | |
| Reporting group title | Selepressin Pooled |
| Reporting group description: All selepressin arms pooled together and treated as a single arm. | |
| Subject analysis set title | Full analysis set |
| Subject analysis set type | Full analysis |
| Subject analysis set description: The FAS comprised of all the subjects who were enrolled (i.e. randomised [as planned]) and dosed. | |
| Subject analysis set title | Selepressin Pooled |
| Subject analysis set type | Full analysis |
| Subject analysis set description: All selepressin arms pooled together and treated as a single arm. | |

Primary: Vasopressor- and Mechanical Ventilator-free Days (PVFDs)

| | |
|-----------------|---|
| End point title | Vasopressor- and Mechanical Ventilator-free Days (PVFDs) ^[1] |
|-----------------|---|

End point description:

Composite endpoint defined as number of days from start of treatment to 30 days thereafter during which subject is:

1. Alive. However, if patient dies within these 30-days then PVFDs will be zero even if there is a period during which subject is alive and free of both vasopressor treatment and mechanical ventilation;
2. Free of treatment with vasopressors: Less than 60 min during any contiguous 24-h period. If a patient requires vasopressors longer than 60 min in total during any 24-h period, the intervening intervals during which they are free of vasopressors will not be included in the determination of PVFDs;
3. Free of any mechanical ventilation: Less than 60 min during any contiguous 24-h period. If a patient requires mechanical ventilation longer than 60 min in total during any 24-h period, the intervening intervals during which they are not receiving mechanical ventilation will not be included in the period free of mechanical ventilation in the determination of PVFDs.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Up to Day 30

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The statistical analysis was pre-planned to be performed only on the Placebo arm and the Selepressin Pooled arm, and not for all the arms as detailed in the statistical analysis plan of this trial. Therefore, the results for this endpoint are reported only for these two arms.

| End point values | Placebo | Selepressin Pooled | | |
|--|------------------------|------------------------|--|--|
| Subject group type | Reporting group | Subject analysis set | | |
| Number of subjects analysed | 266 | 562 | | |
| Units: days | | | | |
| least squares mean (confidence interval 95%) | 14.45 (12.82 to 16.09) | 15.00 (13.77 to 16.23) | | |

Statistical analyses

| | |
|----------------------------|-----------------------------|
| Statistical analysis title | Placebo, Selepressin Pooled |
|----------------------------|-----------------------------|

Statistical analysis description:

The primary endpoint was analysed using a van Elteren test. The analysis included a test of superiority using a two-sided 5% significance level.

| | |
|-------------------|------------------------------|
| Comparison groups | Placebo v Selepressin Pooled |
|-------------------|------------------------------|

| | |
|---|-----|
| Number of subjects included in analysis | 828 |
|---|-----|

| | |
|------------------------|---------------|
| Analysis specification | Pre-specified |
|------------------------|---------------|

| | |
|---------------|-------------|
| Analysis type | superiority |
|---------------|-------------|

| | |
|---------|----------|
| P-value | = 0.3015 |
|---------|----------|

| | |
|--------|------------------|
| Method | van Elteren test |
|--------|------------------|

| | |
|--------------------|----------------------|
| Parameter estimate | Treatment difference |
|--------------------|----------------------|

| | |
|----------------|------|
| Point estimate | 0.55 |
|----------------|------|

Confidence interval

| | |
|-------|------|
| level | 95 % |
|-------|------|

| | |
|-------|---------|
| sides | 2-sided |
|-------|---------|

| | |
|-------------|-------|
| lower limit | -1.34 |
|-------------|-------|

| | |
|-------------|------|
| upper limit | 2.43 |
|-------------|------|

Secondary: All-cause Mortality

| | |
|------------------------|--|
| End point title | All-cause Mortality ^[2] |
| End point description: | Defined as the fraction of subjects that have died, regardless of cause. |
| End point type | Secondary |
| End point timeframe: | At Day 90 |

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The statistical analysis was pre-planned to be performed only on the Placebo arm and the Selepressin Pooled arm, and not for all the arms as detailed in the statistical analysis plan of this trial. Therefore, the results for this endpoint are reported only for these two arms.

| End point values | Placebo | Selepressin Pooled | | |
|-----------------------------|-----------------|----------------------|--|--|
| Subject group type | Reporting group | Subject analysis set | | |
| Number of subjects analysed | 257 | 526 | | |
| Units: percent | | | | |
| number (not applicable) | 39.44 | 40.59 | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Placebo, Selepressin Pooled |
| Statistical analysis description: | Mortality was analysed using a logistic regression model with the individual sequential organ failure assessment (SOFA) scores and age as covariates and treatment arm as factor. |
| Comparison groups | Placebo v Selepressin Pooled |
| Number of subjects included in analysis | 783 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[3] |
| P-value | = 0.7694 |
| Method | Logistic regression |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.049 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.762 |
| upper limit | 1.445 |

Notes:

[3] - An odds ratio < 1 in proportion of subjects dying indicates lower mortality in the selepressin group.

Secondary: Renal Replacement Therapy (RRT)-free Days

| | |
|------------------------|---|
| End point title | Renal Replacement Therapy (RRT)-free Days ^[4] |
| End point description: | RRT-free days was defined as the number of days a subject is free of treatment with any form of RRT |

(continuous RRT, intermittent haemodialysis or peritoneal dialysis) and the intermittent periods were not included.

RRT-free days was analysed excluding subjects on RRT for chronic renal failure at time of randomisation.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Up to Day 30 | |

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The statistical analysis was pre-planned to be performed only on the Placebo arm and the Selepressin Pooled arm, and not for all the arms as detailed in the statistical analysis plan of this trial. Therefore, the results for this endpoint are reported only for these two arms.

| End point values | Placebo | Selepressin Pooled | | |
|--|------------------------|------------------------|--|--|
| Subject group type | Reporting group | Subject analysis set | | |
| Number of subjects analysed | 261 | 550 | | |
| Units: days | | | | |
| least squares mean (confidence interval 95%) | 18.21 (16.14 to 20.29) | 18.50 (17.03 to 19.98) | | |

Statistical analyses

| | |
|----------------------------|-----------------------------|
| Statistical analysis title | Placebo, Selepressin Pooled |
|----------------------------|-----------------------------|

Statistical analysis description:

This endpoint was analysed using a van Elteren test. The analysis was a test of superiority using a two-sided 5% significance level.

| | |
|---|------------------------------|
| Comparison groups | Placebo v Selepressin Pooled |
| Number of subjects included in analysis | 811 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.8458 |
| Method | van Elteren test |
| Parameter estimate | Treatment difference |
| Point estimate | 0.29 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -2.07 |
| upper limit | 2.65 |

Secondary: Intensive Care Unit (ICU)-free Days

| | |
|-----------------|--|
| End point title | Intensive Care Unit (ICU)-free Days ^[5] |
|-----------------|--|

End point description:

The ICU free days, as for the PVFDs, reflect the time from last discharge of the ICU to Day 30 with an absolute penalty for mortality, i.e., any subject that died within this 30-day period was assigned zero value).

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Up to Day 30

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The statistical analysis was pre-planned to be performed only on the Placebo arm and the Selepressin Pooled arm, and not for all the arms as detailed in the statistical analysis plan of this trial. Therefore, the results for this endpoint are reported only for these two arms.

| End point values | Placebo | Selepressin Pooled | | |
|--|------------------------|------------------------|--|--|
| Subject group type | Reporting group | Subject analysis set | | |
| Number of subjects analysed | 266 | 562 | | |
| Units: days | | | | |
| least squares mean (confidence interval 95%) | 12.15 (10.66 to 13.64) | 12.64 (11.51 to 13.76) | | |

Statistical analyses

| Statistical analysis title | Placebo, Selepressin Pooled |
|-----------------------------------|-----------------------------|
|-----------------------------------|-----------------------------|

Statistical analysis description:

This endpoint was analysed using a van Elteren test. The analysis was a test of superiority using a two-sided 5% significance level.

| | |
|---|------------------------------|
| Comparison groups | Placebo v Selepressin Pooled |
| Number of subjects included in analysis | 828 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.4124 |
| Method | van Elteren test |
| Parameter estimate | Treatment difference |
| Point estimate | 0.49 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.22 |
| upper limit | 2.19 |

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment-emergent adverse events (TEAEs) occurring after the investigational medicinal product (IMP) infusion to within 12 hours after the IMP infusion was stopped.

Adverse event reporting additional description:

TEAEs were defined as adverse events that occurred after the IMP infusion to within 12 hours after the IMP infusion was stopped. All treated subjects were included in the safety analysis set and were analysed according to the actual treatment received.

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 20.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

Sterile 0.9% sodium chloride solution given as an infusion.

| | |
|-----------------------|---------------------------|
| Reporting group title | Selepressin 2.5 ng/kg/Min |
|-----------------------|---------------------------|

Reporting group description:

Starting dose: 1.7 ng/kg/min selepressin; Maximum dose: 2.5 ng/kg/min selepressin, given as an infusion.

| | |
|-----------------------|----------------------------|
| Reporting group title | Selepressin 3.75 ng/kg/Min |
|-----------------------|----------------------------|

Reporting group description:

Starting dose: 2.5 ng/kg/min selepressin; Maximum dose: 3.75 ng/kg/min selepressin, given as an infusion.

| | |
|-----------------------|----------------------------|
| Reporting group title | Selepressin 5.25 ng/kg/Min |
|-----------------------|----------------------------|

Reporting group description:

Starting dose: 3.5 ng/kg/min selepressin; Maximum dose: 5.25 ng/kg/min selepressin, given as an infusion.

| Serious adverse events | Placebo | Selepressin 2.5 ng/kg/Min | Selepressin 3.75 ng/kg/Min |
|---|-------------------|---------------------------|----------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 85 / 266 (31.95%) | 57 / 191 (29.84%) | 65 / 177 (36.72%) |
| number of deaths (all causes) | 58 | 43 | 40 |
| number of deaths resulting from adverse events | 58 | 43 | 40 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Lung adenocarcinoma | | | |
| subjects affected / exposed | 1 / 266 (0.38%) | 0 / 191 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lung cancer metastatic | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 266 (0.38%) | 0 / 191 (0.00%) | 1 / 177 (0.56%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Lymphoma | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 191 (0.00%) | 1 / 177 (0.56%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Malignant neoplasm progression | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 1 / 191 (0.52%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Metastatic carcinoma of the bladder | | | |
| subjects affected / exposed | 1 / 266 (0.38%) | 0 / 191 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Metastatic neoplasm | | | |
| subjects affected / exposed | 1 / 266 (0.38%) | 0 / 191 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Pancreatic carcinoma | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 1 / 191 (0.52%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Vascular disorders | | | |
| Circulatory collapse | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 1 / 191 (0.52%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Distributive shock | | | |
| subjects affected / exposed | 1 / 266 (0.38%) | 0 / 191 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Dry gangrene | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 191 (0.00%) | 1 / 177 (0.56%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Extremity necrosis | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 191 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypertension | | | |
| subjects affected / exposed | 1 / 266 (0.38%) | 0 / 191 (0.00%) | 1 / 177 (0.56%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypotension | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 191 (0.00%) | 1 / 177 (0.56%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Ischaemia | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 191 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Poor peripheral circulation | | | |
| subjects affected / exposed | 1 / 266 (0.38%) | 0 / 191 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Shock | | | |
| subjects affected / exposed | 4 / 266 (1.50%) | 1 / 191 (0.52%) | 1 / 177 (0.56%) |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 4 | 0 / 1 | 1 / 1 |
| Shock haemorrhagic | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 191 (0.00%) | 1 / 177 (0.56%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Thrombosis | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 191 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vasoconstriction | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 1 / 191 (0.52%) | 1 / 177 (0.56%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| Peripheral ischaemia | | | |
| subjects affected / exposed | 1 / 266 (0.38%) | 1 / 191 (0.52%) | 4 / 177 (2.26%) |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | 2 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| General disorders and administration site conditions | | | |
| Catheter site haemorrhage | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 1 / 191 (0.52%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Disease progression | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 1 / 191 (0.52%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| General physical health deterioration | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 1 / 191 (0.52%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Hyperthermia | | | |
| subjects affected / exposed | 1 / 266 (0.38%) | 0 / 191 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Multiple organ dysfunction syndrome | | | |
| subjects affected / exposed | 24 / 266 (9.02%) | 10 / 191 (5.24%) | 17 / 177 (9.60%) |
| occurrences causally related to treatment / all | 0 / 24 | 0 / 10 | 0 / 17 |
| deaths causally related to treatment / all | 0 / 24 | 0 / 10 | 0 / 17 |
| Organ failure | | | |

| | | | |
|--|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 191 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute respiratory distress syndrome | | | |
| subjects affected / exposed | 4 / 266 (1.50%) | 3 / 191 (1.57%) | 3 / 177 (1.69%) |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 3 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 1 |
| Acute respiratory failure | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 191 (0.00%) | 1 / 177 (0.56%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Aspiration | | | |
| subjects affected / exposed | 1 / 266 (0.38%) | 0 / 191 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypoxia | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 1 / 191 (0.52%) | 2 / 177 (1.13%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 2 |
| Mediastinal mass | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 1 / 191 (0.52%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Pulmonary fibrosis | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 1 / 191 (0.52%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Pulmonary haemorrhage | | | |
| subjects affected / exposed | 1 / 266 (0.38%) | 0 / 191 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory failure | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 3 / 266 (1.13%) | 0 / 191 (0.00%) | 1 / 177 (0.56%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| Investigations | | | |
| Cardiac output decreased | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 191 (0.00%) | 1 / 177 (0.56%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Troponin I increased | | | |
| subjects affected / exposed | 1 / 266 (0.38%) | 0 / 191 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Troponin increased | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 191 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Anastomotic leak | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 2 / 191 (1.05%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Endotracheal intubation complication | | | |
| subjects affected / exposed | 1 / 266 (0.38%) | 0 / 191 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Subarachnoid haemorrhage | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 191 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Traumatic haemothorax | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 191 (0.00%) | 1 / 177 (0.56%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Cardiac disorders | | | |
| Acute coronary syndrome | | | |
| subjects affected / exposed | 1 / 266 (0.38%) | 1 / 191 (0.52%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 2 / 191 (1.05%) | 1 / 177 (0.56%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atrial fibrillation | | | |
| subjects affected / exposed | 1 / 266 (0.38%) | 0 / 191 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac arrest | | | |
| subjects affected / exposed | 3 / 266 (1.13%) | 5 / 191 (2.62%) | 5 / 177 (2.82%) |
| occurrences causally related to treatment / all | 1 / 3 | 4 / 7 | 0 / 6 |
| deaths causally related to treatment / all | 1 / 2 | 1 / 2 | 0 / 0 |
| Cardiac failure | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 191 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiogenic shock | | | |
| subjects affected / exposed | 1 / 266 (0.38%) | 1 / 191 (0.52%) | 1 / 177 (0.56%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| Cyanosis | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 191 (0.00%) | 1 / 177 (0.56%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Defect conduction intraventricular | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 1 / 191 (0.52%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| Myocardial depression | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 191 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myocardial infarction | | | |
| subjects affected / exposed | 1 / 266 (0.38%) | 0 / 191 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myocardial ischaemia | | | |
| subjects affected / exposed | 1 / 266 (0.38%) | 1 / 191 (0.52%) | 4 / 177 (2.26%) |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | 4 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myocardial stunning | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 191 (0.00%) | 1 / 177 (0.56%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulseless electrical activity | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 191 (0.00%) | 2 / 177 (1.13%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Right ventricular failure | | | |
| subjects affected / exposed | 1 / 266 (0.38%) | 0 / 191 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sinus bradycardia | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 191 (0.00%) | 1 / 177 (0.56%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Supraventricular tachycardia | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 191 (0.00%) | 1 / 177 (0.56%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tachycardia | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 266 (0.38%) | 0 / 191 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ventricular arrhythmia | | | |
| subjects affected / exposed | 1 / 266 (0.38%) | 0 / 191 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| Ventricular fibrillation | | | |
| subjects affected / exposed | 1 / 266 (0.38%) | 0 / 191 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ventricular tachycardia | | | |
| subjects affected / exposed | 1 / 266 (0.38%) | 0 / 191 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Brain oedema | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 191 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebral ischaemia | | | |
| subjects affected / exposed | 1 / 266 (0.38%) | 1 / 191 (0.52%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| Coma | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 191 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Encephalopathy | | | |
| subjects affected / exposed | 2 / 266 (0.75%) | 0 / 191 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Vasculitis cerebral | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 266 (0.38%) | 0 / 191 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 191 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Disseminated intravascular coagulation | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 191 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemolysis | | | |
| subjects affected / exposed | 1 / 266 (0.38%) | 0 / 191 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Splenic necrosis | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 191 (0.00%) | 1 / 177 (0.56%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thrombocytopenia | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 191 (0.00%) | 1 / 177 (0.56%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Abdominal compartment syndrome | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 191 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colitis ischaemic | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 191 (0.00%) | 1 / 177 (0.56%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Colonic fistula | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 191 (0.00%) | 1 / 177 (0.56%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Duodenal perforation | | | |
| subjects affected / exposed | 1 / 266 (0.38%) | 0 / 191 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastric haemorrhage | | | |
| subjects affected / exposed | 1 / 266 (0.38%) | 0 / 191 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal ischaemia | | | |
| subjects affected / exposed | 1 / 266 (0.38%) | 0 / 191 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal necrosis | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 1 / 191 (0.52%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| Ileus | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 191 (0.00%) | 1 / 177 (0.56%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Intestinal ischaemia | | | |
| subjects affected / exposed | 3 / 266 (1.13%) | 4 / 191 (2.09%) | 1 / 177 (0.56%) |
| occurrences causally related to treatment / all | 2 / 3 | 3 / 4 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 1 | 2 / 3 | 1 / 1 |
| Large intestine perforation | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 191 (0.00%) | 1 / 177 (0.56%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peritoneal haemorrhage | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 266 (0.38%) | 0 / 191 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Acute hepatic failure | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 1 / 191 (0.52%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| Cholecystitis | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 191 (0.00%) | 1 / 177 (0.56%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Chronic hepatic failure | | | |
| subjects affected / exposed | 1 / 266 (0.38%) | 0 / 191 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Gallbladder disorder | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 191 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatic failure | | | |
| subjects affected / exposed | 1 / 266 (0.38%) | 1 / 191 (0.52%) | 1 / 177 (0.56%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Hepatitis acute | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 1 / 191 (0.52%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Hepatocellular injury | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 1 / 191 (0.52%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ischaemic hepatitis | | | |

| | | | |
|--|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 191 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| Skin discolouration | | | |
| subjects affected / exposed | 1 / 266 (0.38%) | 2 / 191 (1.05%) | 2 / 177 (1.13%) |
| occurrences causally related to treatment / all | 1 / 1 | 2 / 2 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 5 / 266 (1.88%) | 0 / 191 (0.00%) | 2 / 177 (1.13%) |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal failure | | | |
| subjects affected / exposed | 1 / 266 (0.38%) | 1 / 191 (0.52%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Fasciitis | | | |
| subjects affected / exposed | 1 / 266 (0.38%) | 0 / 191 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Abscess | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 191 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Arthritis infective | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 1 / 191 (0.52%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cellulitis | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 191 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Device related sepsis | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 191 (0.00%) | 1 / 177 (0.56%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Endocarditis | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 1 / 191 (0.52%) | 1 / 177 (0.56%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Extradural abscess | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 191 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Klebsiella sepsis | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 191 (0.00%) | 1 / 177 (0.56%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Necrotising fasciitis | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 191 (0.00%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peritonitis bacterial | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 1 / 191 (0.52%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 4 / 266 (1.50%) | 2 / 191 (1.05%) | 2 / 177 (1.13%) |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sepsis | | | |

| | | | |
|---|------------------|------------------|------------------|
| subjects affected / exposed | 1 / 266 (0.38%) | 0 / 191 (0.00%) | 1 / 177 (0.56%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| Septic shock | | | |
| subjects affected / exposed | 15 / 266 (5.64%) | 10 / 191 (5.24%) | 12 / 177 (6.78%) |
| occurrences causally related to treatment / all | 1 / 15 | 0 / 10 | 0 / 12 |
| deaths causally related to treatment / all | 1 / 14 | 0 / 9 | 0 / 9 |
| Metabolism and nutrition disorders | | | |
| Hyperkalaemia | | | |
| subjects affected / exposed | 1 / 266 (0.38%) | 0 / 191 (0.00%) | 1 / 177 (0.56%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Hyperlactacidaemia | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 1 / 191 (0.52%) | 0 / 177 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lactic acidosis | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 191 (0.00%) | 1 / 177 (0.56%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |

| Serious adverse events | Selepressin 5.25 ng/kg/Min | | |
|---|-------------------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 57 / 194 (29.38%) | | |
| number of deaths (all causes) | 42 | | |
| number of deaths resulting from adverse events | 42 | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Lung adenocarcinoma | | | |
| subjects affected / exposed | 0 / 194 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Lung cancer metastatic | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 0 / 194 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Lymphoma | | | |
| subjects affected / exposed | 0 / 194 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Malignant neoplasm progression | | | |
| subjects affected / exposed | 0 / 194 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metastatic carcinoma of the bladder | | | |
| subjects affected / exposed | 0 / 194 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metastatic neoplasm | | | |
| subjects affected / exposed | 0 / 194 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pancreatic carcinoma | | | |
| subjects affected / exposed | 0 / 194 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vascular disorders | | | |
| Circulatory collapse | | | |
| subjects affected / exposed | 0 / 194 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Distributive shock | | | |
| subjects affected / exposed | 0 / 194 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Dry gangrene | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 0 / 194 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Extremity necrosis | | | |
| subjects affected / exposed | 1 / 194 (0.52%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 1 / 1 | | |
| Hypertension | | | |
| subjects affected / exposed | 0 / 194 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypotension | | | |
| subjects affected / exposed | 3 / 194 (1.55%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 2 | | |
| Ischaemia | | | |
| subjects affected / exposed | 1 / 194 (0.52%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Poor peripheral circulation | | | |
| subjects affected / exposed | 0 / 194 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Shock | | | |
| subjects affected / exposed | 3 / 194 (1.55%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 3 | | |
| Shock haemorrhagic | | | |
| subjects affected / exposed | 1 / 194 (0.52%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Thrombosis | | | |

| | | | |
|--|------------------|--|--|
| subjects affected / exposed | 1 / 194 (0.52%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vasoconstriction | | | |
| subjects affected / exposed | 0 / 194 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Peripheral ischaemia | | | |
| subjects affected / exposed | 2 / 194 (1.03%) | | |
| occurrences causally related to treatment / all | 1 / 2 | | |
| deaths causally related to treatment / all | 1 / 1 | | |
| General disorders and administration site conditions | | | |
| Catheter site haemorrhage | | | |
| subjects affected / exposed | 0 / 194 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Disease progression | | | |
| subjects affected / exposed | 0 / 194 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General physical health deterioration | | | |
| subjects affected / exposed | 0 / 194 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hyperthermia | | | |
| subjects affected / exposed | 0 / 194 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Multiple organ dysfunction syndrome | | | |
| subjects affected / exposed | 12 / 194 (6.19%) | | |
| occurrences causally related to treatment / all | 0 / 12 | | |
| deaths causally related to treatment / all | 0 / 12 | | |
| Organ failure | | | |

| | | | |
|--|-----------------|--|--|
| subjects affected / exposed | 1 / 194 (0.52%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute respiratory distress syndrome | | | |
| subjects affected / exposed | 1 / 194 (0.52%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Acute respiratory failure | | | |
| subjects affected / exposed | 0 / 194 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Aspiration | | | |
| subjects affected / exposed | 0 / 194 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypoxia | | | |
| subjects affected / exposed | 0 / 194 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Mediastinal mass | | | |
| subjects affected / exposed | 0 / 194 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pulmonary fibrosis | | | |
| subjects affected / exposed | 0 / 194 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pulmonary haemorrhage | | | |
| subjects affected / exposed | 0 / 194 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory failure | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 5 / 194 (2.58%) | | |
| occurrences causally related to treatment / all | 1 / 5 | | |
| deaths causally related to treatment / all | 1 / 3 | | |
| Investigations | | | |
| Cardiac output decreased | | | |
| subjects affected / exposed | 0 / 194 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Troponin I increased | | | |
| subjects affected / exposed | 0 / 194 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Troponin increased | | | |
| subjects affected / exposed | 1 / 194 (0.52%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Injury, poisoning and procedural complications | | | |
| Anastomotic leak | | | |
| subjects affected / exposed | 0 / 194 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Endotracheal intubation complication | | | |
| subjects affected / exposed | 0 / 194 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Subarachnoid haemorrhage | | | |
| subjects affected / exposed | 1 / 194 (0.52%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Traumatic haemothorax | | | |
| subjects affected / exposed | 0 / 194 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|-----------------|--|--|
| Cardiac disorders | | | |
| Acute coronary syndrome | | | |
| subjects affected / exposed | 0 / 194 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 0 / 194 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 194 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac arrest | | | |
| subjects affected / exposed | 1 / 194 (0.52%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac failure | | | |
| subjects affected / exposed | 2 / 194 (1.03%) | | |
| occurrences causally related to treatment / all | 1 / 2 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Cardiogenic shock | | | |
| subjects affected / exposed | 0 / 194 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cyanosis | | | |
| subjects affected / exposed | 2 / 194 (1.03%) | | |
| occurrences causally related to treatment / all | 2 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Defect conduction intraventricular | | | |
| subjects affected / exposed | 0 / 194 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Myocardial depression | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 194 (0.52%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Myocardial infarction | | | |
| subjects affected / exposed | 1 / 194 (0.52%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Myocardial ischaemia | | | |
| subjects affected / exposed | 0 / 194 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Myocardial stunning | | | |
| subjects affected / exposed | 0 / 194 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pulseless electrical activity | | | |
| subjects affected / exposed | 1 / 194 (0.52%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Right ventricular failure | | | |
| subjects affected / exposed | 0 / 194 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Sinus bradycardia | | | |
| subjects affected / exposed | 0 / 194 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Supraventricular tachycardia | | | |
| subjects affected / exposed | 1 / 194 (0.52%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Tachycardia | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 0 / 194 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Ventricular arrhythmia | | | |
| subjects affected / exposed | 0 / 194 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Ventricular fibrillation | | | |
| subjects affected / exposed | 0 / 194 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Ventricular tachycardia | | | |
| subjects affected / exposed | 1 / 194 (0.52%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Nervous system disorders | | | |
| Brain oedema | | | |
| subjects affected / exposed | 1 / 194 (0.52%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Cerebral ischaemia | | | |
| subjects affected / exposed | 0 / 194 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Coma | | | |
| subjects affected / exposed | 1 / 194 (0.52%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Encephalopathy | | | |
| subjects affected / exposed | 1 / 194 (0.52%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Vasculitis cerebral | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 0 / 194 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 1 / 194 (0.52%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Disseminated intravascular coagulation | | | |
| subjects affected / exposed | 1 / 194 (0.52%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Haemolysis | | | |
| subjects affected / exposed | 0 / 194 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Splenic necrosis | | | |
| subjects affected / exposed | 0 / 194 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 0 / 194 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Abdominal compartment syndrome | | | |
| subjects affected / exposed | 1 / 194 (0.52%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Colitis ischaemic | | | |
| subjects affected / exposed | 0 / 194 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | | |
|---|-----------------|--|--|--|
| Colonic fistula | | | | |
| subjects affected / exposed | 0 / 194 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Duodenal perforation | | | | |
| subjects affected / exposed | 0 / 194 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastric haemorrhage | | | | |
| subjects affected / exposed | 0 / 194 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastrointestinal ischaemia | | | | |
| subjects affected / exposed | 0 / 194 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastrointestinal necrosis | | | | |
| subjects affected / exposed | 0 / 194 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Ileus | | | | |
| subjects affected / exposed | 0 / 194 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Intestinal ischaemia | | | | |
| subjects affected / exposed | 2 / 194 (1.03%) | | | |
| occurrences causally related to treatment / all | 1 / 3 | | | |
| deaths causally related to treatment / all | 1 / 2 | | | |
| Large intestine perforation | | | | |
| subjects affected / exposed | 0 / 194 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Peritoneal haemorrhage | | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 0 / 194 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatobiliary disorders | | | |
| Acute hepatic failure | | | |
| subjects affected / exposed | 0 / 194 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cholecystitis | | | |
| subjects affected / exposed | 0 / 194 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Chronic hepatic failure | | | |
| subjects affected / exposed | 0 / 194 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gallbladder disorder | | | |
| subjects affected / exposed | 1 / 194 (0.52%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatic failure | | | |
| subjects affected / exposed | 0 / 194 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatitis acute | | | |
| subjects affected / exposed | 0 / 194 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatocellular injury | | | |
| subjects affected / exposed | 0 / 194 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Ischaemic hepatitis | | | |

| | | | |
|--|-----------------|--|--|
| subjects affected / exposed | 1 / 194 (0.52%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Skin and subcutaneous tissue disorders | | | |
| Skin discolouration | | | |
| subjects affected / exposed | 1 / 194 (0.52%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 0 / 194 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal failure | | | |
| subjects affected / exposed | 2 / 194 (1.03%) | | |
| occurrences causally related to treatment / all | 1 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Fasciitis | | | |
| subjects affected / exposed | 0 / 194 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Abscess | | | |
| subjects affected / exposed | 1 / 194 (0.52%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Arthritis infective | | | |
| subjects affected / exposed | 0 / 194 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cellulitis | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 194 (0.52%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Device related sepsis | | | |
| subjects affected / exposed | 0 / 194 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Endocarditis | | | |
| subjects affected / exposed | 1 / 194 (0.52%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Extradural abscess | | | |
| subjects affected / exposed | 1 / 194 (0.52%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Klebsiella sepsis | | | |
| subjects affected / exposed | 0 / 194 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Necrotising fasciitis | | | |
| subjects affected / exposed | 1 / 194 (0.52%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Peritonitis bacterial | | | |
| subjects affected / exposed | 0 / 194 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 194 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Sepsis | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 3 / 194 (1.55%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 2 | | |
| Septic shock | | | |
| subjects affected / exposed | 8 / 194 (4.12%) | | |
| occurrences causally related to treatment / all | 0 / 8 | | |
| deaths causally related to treatment / all | 0 / 7 | | |
| Metabolism and nutrition disorders | | | |
| Hyperkalaemia | | | |
| subjects affected / exposed | 0 / 194 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hyperlactacidaemia | | | |
| subjects affected / exposed | 0 / 194 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Lactic acidosis | | | |
| subjects affected / exposed | 0 / 194 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | Placebo | Selepressin 2.5 ng/kg/Min | Selepressin 3.75 ng/kg/Min |
|--|-------------------|------------------------------|-------------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 94 / 266 (35.34%) | 54 / 191 (28.27%) | 63 / 177 (35.59%) |
| Injury, poisoning and procedural complications | | | |
| Expired product administered | | | |
| subjects affected / exposed | 50 / 266 (18.80%) | 26 / 191 (13.61%) | 29 / 177 (16.38%) |
| occurrences (all) | 94 | 48 | 47 |
| Cardiac disorders | | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 30 / 266 (11.28%) | 22 / 191 (11.52%) | 24 / 177 (13.56%) |
| occurrences (all) | 43 | 23 | 27 |

| | | | |
|--------------------------------------|------------------|------------------|------------------|
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 24 / 266 (9.02%) | 12 / 191 (6.28%) | 6 / 177 (3.39%) |
| occurrences (all) | 25 | 13 | 6 |
| Thrombocytopenia | | | |
| subjects affected / exposed | 12 / 266 (4.51%) | 9 / 191 (4.71%) | 10 / 177 (5.65%) |
| occurrences (all) | 13 | 9 | 10 |
| Metabolism and nutrition disorders | | | |
| Hypokalaemia | | | |
| subjects affected / exposed | 4 / 266 (1.50%) | 5 / 191 (2.62%) | 9 / 177 (5.08%) |
| occurrences (all) | 4 | 5 | 9 |

| | | | |
|--|-------------------------------|--|--|
| Non-serious adverse events | Selepressin 5.25 ng/kg/Min | | |
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 60 / 194 (30.93%) | | |
| Injury, poisoning and procedural complications | | | |
| Expired product administered | | | |
| subjects affected / exposed | 31 / 194 (15.98%) | | |
| occurrences (all) | 62 | | |
| Cardiac disorders | | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 22 / 194 (11.34%) | | |
| occurrences (all) | 29 | | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 7 / 194 (3.61%) | | |
| occurrences (all) | 7 | | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 11 / 194 (5.67%) | | |
| occurrences (all) | 11 | | |
| Metabolism and nutrition disorders | | | |
| Hypokalaemia | | | |
| subjects affected / exposed | 4 / 194 (2.06%) | | |
| occurrences (all) | 4 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|--------------|---|
| 08 July 2016 | <p>This was a substantial amendment, which was implemented during the conduct of the trial. The main reasons for this protocol amendment were to implement the following changes to the protocol:</p> <ul style="list-style-type: none"><li data-bbox="416 445 1426 506">• To allow use of infusion pumps for administration of the investigational medicinal product.<li data-bbox="416 506 1426 618">• To allow for calcium (free or total), creatinine (plasma or serum), and troponin (I or T) measurements according to local clinical practice. Uric acid was not routinely measured in clinical practice and therefore, uric acid was no longer required to be collected.<li data-bbox="416 618 1426 730">• To introduce the recording of the highest lactate level obtained in accordance with local clinical practice in the pre-IMP treatment period following start of vasopressor treatment and to clarify that venous lactate could be recorded if arterial lactate had not been measured. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported