**Source data location description** (version 2023-10-09)

*#Please specify which medical record (for example Melior) and where the data (for example laboratory data) can be found.*

| **Variable** | **Definition** | **Source #** | **Comment** |
| --- | --- | --- | --- |
| **Primary outcome** | All-cause mortality at 90 days |  |  |
| **Secondary outcomes** | One or more complications in the ICU defined as one or more of the following events in the ICU:  a) Acute cerebral infarction documented on MRI or CT scans of the brain AND corresponding neurological symptoms  b) Acute coronary syndrome (a diagnosis of acute myocardial infarction or unstable angina pectoris) AND reperfusion treatment (percutaneous coronary intervention [PCI]/thrombolysis) or initiated/increased antithrombotic treatment  c) Acute intestinal infarction diagnosed during surgery or by angiography.  d) Limb ischemia defined as clinical signs of limb ischemia AND treatment [open/percutaneous vascular intervention, amputation, or initiation/increased antithrombotic treatment]  e) New onset severe acute kidney injury (stage 3 according to the kidney disease improving global outcomes (KIDIGO) criteria). |  |  |
| Days alive and free of mechanical ventilation within 90 days of inclusion. |  |  |
| Cognitive function measured using the Montreal Cognitive Assessment BLIND test (MoCA-BLIND) at 6 months |  |  |
| Health-Related Quality of Life using the European Quality of Life visual analogue scale (EQ-VAS) at 6 months. |  |  |
| **Explorative outcomes** | Days alive and free of renal replacement therapy (RRT) within 90-days of inclusion. |  |  |
| The composite of death, new receipt of renal replacement therapy, or persistent renal dysfunction (defined as a final inpatient creatinine value ≥200% of the baseline value) |  |  |
| Cumulative dose of diuretics during the first 5 days after randomisation (defined daily doses according to the World Health Organization). |  |  |
| Glasgow Outcome Scale Extended (GOSE) at 6 months. |  |  |
| European Quality of Life visual 5 dimension- 5 level scale (EQ-5D-5L) at 6 months. |  |  |
| WHO Disability Assessment Schedule (WHODAS) 2.0 (12 item version) at 6 months. |  |  |
| Modified Fatigue Impact Scale (MFIS) at 6 months. |  |  |
| All-cause mortality at 12 months. |  |  |
| Days alive and out of hospital within 90-days of inclusion |  |  |
| Hypoglycaemia (≤ 3.9 mmol/l) |  |  |
| Electrolyte disturbances (hypernatremia > 159 mmol/L) |  |  |
| Acid base disturbances (hyperchloremic acidosis pH < 7.15 and plasma Cl- > 115) |  |  |
| Metabolic alkalosis pH > 7.59 and S-BE > 9. |  |  |
| Central venous catheter-related complications that could potentially be related to concentrated drugs given in the intervention group (for example, thrombosis, stenosis, malfunction, and infections) |  |  |
| **Variables collected at screening** | Age (years) |  |  |
| Sex (F/M) |  |  |
| Gender (F/M/other) |  |  |
| Lactate (highest value while the patient is in the ICU and receiving vasopressors, up to 12h after admission) |  |  |
| Date and time of ICU admission (dd-mmm-yyyy, hh:mm) |  |  |
| Septic shock according to the Sepsis 3 criteria within 12 hours of ICU admission (suspected or confirmed infection, change in sequential organ failure assessment score [SOFA] by 2 points or more from baseline, plasma lactate above 2 mmol/L, and infusion of vasopressor/inotrope to maintain mean arterial pressure of 65mmHg or above despite adequate fluid resuscitation) and need for vasopressors at the time of inclusion. |  |  |
| Exclusion Criteria:   1. Confirmed or suspected pregnancy 2. Previous inclusion in the trial |  |  |
| **Consent information** | Patient informed (Y/N) and date (dd-mmm-yyyy)  - Date informed (if Y)  - Reason not informed (if N) |  |  |
| Patient consented (Y/N) |  |  |
| Consent withdrawn (Y/N)  - Date of withdrawal (dd-mmm-yyyy)  - Can the data be used (Y/N)  - Can primary outcome be collected (Y/N) |  |  |
| **Demographic/ background variables** | Height (cm) |  |  |
|  | Weight at baseline (kg, standardized according to local practice) |  |  |
|  | Clinical Frailty Score |  |  |
|  | Baseline creatinine [lowest in the 12 months preceding randomization] (µmol/L) |  |  |
|  | Charlson Comorbidity Index |  |  |
|  | Type of initial antibiotic treatment |  |  |
|  | Suspected pathogen   * Suspected pathogen sensitive to initial antibiotic treatment (Y/N) |  |  |
|  | Hospital admission (dd-mmm-yyyy, hh:mm) |  |  |
|  | Hospital location prior to randomization   * Emergency department * Operating room * Other ICU * Other unit |  |  |
|  | Surgery prior to randomization (Y/N), if yes, specify:   * Head and neck * Thorax * Abdominal/pelvic * Extremities * Trauma * Other |  |  |
|  | Origin of sepsis (according to criteria developed by Linder/Mellhammar. Mellhammar et al. Crit Care Exp 2022;4:e0697) |  |  |
| **Baseline ariables at study inclusion** (values closest in time to enrolment, within ± 6 h, unless other timeframe is specified) | Body temperature (degree Celsius) |  |  |
|  | SAPS-III (Simplified acute physiology score-III) |  |  |
|  | Glasgow Coma Scale (GCS) |  |  |
|  | Creatinine (μmol/L) |  |  |
|  | Renal replacement therapy (Y/N) |  |  |
|  | Acute renal injury (Y/N, if yes specify KDIGO score) |  |  |
|  | Bilirubin (μmol/L) |  |  |
|  | Platelet count (x109/ml) |  |  |
|  | Mean arterial pressure (mmHg) |  |  |
|  | Systolic pressure (mmHg) |  |  |
|  | Type of inotropic drug or vasopressor (any dose of dobutamine, dopamine, vasopressin or other V1A agonists, levosimendan, angiotensin II, noradrenaline, adrenaline, milrinone, or other) |  |  |
|  | Noradrenaline dose (highest dose in the 6 hours prior to enrollment; μg/kg/min) |  |  |
|  | Corticosteroid treatment (Y/N) |  |  |
|  | Atrial fibrillation/flutter (Y/N) |  |  |
|  | Ischemic events (Y/N) (criteria described above), if yes, specify: a) Limb, b) Cerebral, c) Heart, d) Intestine |  |  |
|  | Heart rate (bpm) |  |  |
|  | Ventilatory support (nasal catheter, nasal high flow oxygen, Hudson mask or similar, reservoir mask, non-invasive mechanical ventilation, invasive mechanical ventilation [defined as mechanical ventilation through an orotracheal tube or through a tracheostomy], none. Classification at each day will be based on the highest level of support. |  |  |
|  | CRP (g/L) |  |  |
|  | Leucocytes (x109 cells/L) |  |  |
|  | Haemoglobin (g/L) |  |  |
|  | Potassium (mmol/L) |  |  |
|  | Sodium (mmol/L) |  |  |
|  | Chloride (mmol/L) |  |  |
|  | Blood glucose (mmol/L) |  |  |
|  | * FiO2 (%) |  |  |
|  | PaO2 (kPa) |  |  |
|  | PaCO2 (kPa |  |  |
|  | pH |  |  |
|  | Base excess (BE, mEq/L) |  |  |
|  | Volume of fluid intake in the 24h prior to inclusion   * Crystalloids (Ringer’s acetate/lactate [ml], 0.9% NaCl [ml], other [ml], * Colloids (Albumin 4-5% [ml], Albumin 20% [ml], other [ml] * Blood products (Erythrocytes [ml], Plasma [ml]- Platelets [ml]) * Glucose (any concentration) (ml) * Parenteral nutrition (ml) * Enteral nutrition (ml) * Enteral water (ml) |  |  |
| **Daily variables from inclusion to day 5** | Patient in a REDUSE ICU this day (Y/N) |  |  |
| Resuscitation fluids   1. Crystalloids administered to correct hemodynamic impairment as noted in the patient chart or given at a rate > 5 ml/kg/h (Ringer’s acetate/lactate [ml], 0.9% NaCl [ml], other [ml] 2. Colloids (Albumin 4-5% [ml], Albumin 20% [ml], other [ml] 3. Blood products (Erythrocytes [ml], Plasma [ml], Platelets [ml] |  |  |
| Intravenous vehicles and drugs   1. Antibiotics [mL] 2. Inotropes (includes dobutamine, levosimedan, or dopamine <5mcg/kg/min) [mL] 3. Vasopressors [mL] 4. Analgesics [mL] 5. Sedatives [mL] 6. Insulin [mL] and dose [E/24h] 7. Potassium [mL] 8. Other electrolytes [mL] 9. Other drugs [mL] 10. 5% glucose used as a vehicle [mL] 11. Other concentration of glucose used as a vehicle [mL and concentration in %] |  |  |
| Maintenance/replacement and nutrition   1. Crystalloids administered for reasons other than correcting hemodynamic impairment (Ringer’s acetate/lactate [ml], 0.9% NaCl [ml], other (ml), 2. Glucose 2.5% [ml], 5% [ml], 10% [ml], 20% (ml), other glucose strength (mL and concentration in %) 3. Was glucose given for an allowed indication (on days 1-3 in the restrictive group), Parenteral nutrition (ml) 4. Enteral nutrition (ml) 5. Enteral water (ml) 6. Other fluids (mL) 7. Total caloric intake [including Propofol and glucose solutions] (kcal) |  |  |
| Diuretics   1. Loop diuretics/furosemide [mg/24h] 2. Other (type of drug and mg/24h) |  |  |
| Fluid output   1. Urinary output [ml] 2. Drains [ml] 3. Hemorrhage [ml] 4. Faeces [if liquid and collected through a faecal management system, ml] 5. Fluid removal in RRT [ml] 6. Other losses [evaporation excluded] (ml) |  |  |
| Weight (kg) |  |  |
| Fluid balance goal for next 24h (Y/N, and volume in mL) |  |  |
| Creatinine [highest](μmol/L) |  |  |
| Acute renal injury (Y/N, if yes specify KDIGO score) |  |  |
| Renal replacement therapy (Y/N) |  |  |
| Earliest urea (mmol/L) |  |  |
| Lowest MAP (mmHg) |  |  |
| Type of inotropic drug or vasopressor (any dose of dobutamine, dopamine, vasopressin or other V1A agonists, levosimendan, angiotensin II, noradrenaline, adrenaline, milrinone, or other) |  |  |
| Noradrenaline dose (highest dose during the day; μg/kg/min) |  |  |
| Corticosteroid treatment (Y/N) |  |  |
| Atrial fibrillation/flutter (Y/N) |  |  |
| Mechanical ventilation (Y/N) |  |  |
| Lowest PaO2 (kPa) |  |  |
| FiO2 (at time of lowest PaO2; %) |  |  |
| Lactate [highest] (mmol/L) |  |  |
| Sodium [earliest] (mmol/L) |  |  |
| Potassium [earliest] (mmol/L) |  |  |
| Chloride [earliest] (mmol/L) |  |  |
| Blood glucose [earliest] (mmol/L) |  |  |
| Ischemic events (Y/N) (criteria described above) |  |  |
| Safety outcomes   1. Hypoglycemia [< 3.9 mmol/L] (Y/N) 2. Hypernatriemia [>159 mmol/L] (Y/N) 3. Hyperchloremic acidosis [pH<7.15 and plasma-chloride >115 mmol/L] (Y/N) 4. Metabolic alkalosis [pH>7.59 and base excess >9] (Y/N) 5. Central venous catheter complications (Includes malfunctions, infections, thrombosis and venous stenosis) (Y/N) 6. Suspected unexpected complications (SUSAC) (Y/N) |  |  |
| **Daily variables from day 6 to discharge** | Patient in a REDUSE ICU this day (Y/N) |  |  |
| Volume of resuscitation fluids (mL) |  |  |
| Volume of non-resuscitation fluids (mL) |  |  |
| Total fluid output (mL) |  |  |
| Ischemic events (Y/N) (criteria described above), if yes, specify: if yes, specify: a) Limb, b) Cerebral, c)Heart, d) Intestine |  |  |
| Acute renal injury (Y/N, if yes specify KDIGO score) |  |  |
| Safety outcomes   1. Hypoglycemia [< 3.9 mmol/L] (Y/N) 2. Hypernatriemia [>159 mmol/L] (Y/N) 3. Hyperchloremic acidosis [pH<7.15 and plasma-chloride >115 mmol/L] (Y/N) 4. Metabolic alkalosis [pH>7.59 and base excess >9] (Y/N) 5. Central venous catheter complications (Includes malfunctions, infections, thrombosis and venous stenosis) (Y/N)   Suspected unexpected complications (SUSAC) (Y/N) |  |  |
| **Variables at discharge from REDUSE ICU** | ICU discharge   1. Date and time of ICU discharge (dd-mmm-yyyy, hh:mm) 2. Status at ICU discharge (alive/deceased) |  |  |
| Withdrawal of life sustaining therapies (WLST) (Y/N), if yes, specify reason:   1. Irreversible organ failure (Y/N); if yes specify Cardiac, Lung, Liver, Kidney, Coagulation, Brain or Other 2. Medical comorbidity (Y/N) 3. Other (Y/N); specify   Date and time when WLST decision was made (dd-mmm-yyyy, hh:mm) |  |  |
| **Patient transfer** | Patient transferred to (REDUSE ICU or non-REDUSE ICU) |  |  |
| Date of transfer (dd-mmm-yyyy) |  |  |
| **Variables up to 90 days after inclusion** | Date of follow-up |  |  |
| Status (alive/deceased) |  |  |
| Days alive and free of renal replacement therapy (RRT) |  |  |
| Days alive and without invasive mechanical ventilation as defined above |  |  |
| Days alive without vasopressors |  |  |
| Days alive and out of hospital  If deceased, date and time of death (dd-mmm-yyyy, hh:mm) |  |  |
| Creatinine on hospital discharge |  |  |
| **Variables at 6-months** | Date of follow-up |  |  |
| Status (alive/deceased) |  |  |
| Place of follow up (Institution/ home of patient/ telephone/ digital) |  |  |
| Assessments and questionnaires defined in the secondary and exploratory outcomes above |  |  |
| Background information questionnaire |  |  |
| Patient experience questionnaire |  |  |