SOP: List of data needed for eCRF entry

Version	Author(s)	Date	Changes	Approved by
1.0	Johanne Juul Petersen Mathias Lühr Hansen Caroline Kamp	14/02-25	Initial version	Janus Christian Jakobsen
1.1	Patrick Andersen Johanne Juul Petersen	15/09-25	Substudies added and data points clarified	Caroline Kamp
1.2	Jonas Leth Bjerg Caroline Kamp	28/08-26	Cardiovascular substudy added	Caroline Kamp

Content

Data to be reported during screening and randomisation

- Date and time of birth (dd-mm-yyyy and HH:mm)
- Gestational age more than 28 weeks (yes/no)
- Expected to receive invasive mechanical ventilation for at least 24 hours (yes/no)
- Possible to initiate cerebral oximetry within 6 hours from initiation of mechanical ventilation (yes/no)
- Method of consent (prior informed consent, deferred consent, opt-out, consent no sought)
- Suspicion of or confirmed brain injury or disorder (yes/no)
- Suspicion or diagnosis of congenital heart malformation likely to require surgery (yes/no)
- Would you like to randomise the neonate (yes/no)
- Gestational age (lower gestational age (≤ 34 weeks)/higher gestational age (> 34 weeks))
- Surgery as the cause for intubation (yes/no)

Data to be reported at end of monitoring (28 days after birth) for all infants

- Gestational age (weeks+days)
- Birth weight (grams)
- Singleton or multiple birth (singleton/multiple births)
- Sex (male/female)
- Race or ethnic group (White, Black or African American, Asian, Hispanic or Latino, Mixed, Other)
- Apgar score after one minute
- Apgar score after five minutes
- Specify primary reason for tracheal intubation and mechanical ventilation (surgery to allow optimal pain relief/surgery for physiological or anatomical reasons/primary pulmonary problem/other)
- Did the baby receive surfactant therapy at any time until end of monitoring? (yes/no)
- Did the baby receive cardiovascular support at any time until end of monitoring? (yes/no)

Data to be reported at end of monitoring for infants in the cerebral oximetry group

- Did the newborn undergo cerebral oximetry monitoring during the index (first) episode of mechanical ventilation? (yes/no)

If no to oximetry monitoring

- Why did the newborn not undergo cerebral oximetry monitoring? (free text)

If yes to oximetry monitoring

- Was cerebral oximetry monitoring discontinued for more than 12 hours straight? (yes/no)
  If no:
  - Why cerebral oximetry monitoring discontinued for more than 12 hours straight? (free text)
- Time from tracheal initiation and start of mechanical ventilation to cerebral oximetry monitoring (hours)
- Days of cerebral oximetry monitoring during the first (index) episode of mechanical ventilation (days)
- Did clinical staff change the medical management due to cerebral hypoxia (yes/no)
  If yes:
  - Specification of changes in medical management due to cerebral hypoxia (volume expansion/initiation of, or change in vasopressor/inotrope infusion rate/treatment of PDA/red blood cell/transfusion/FiO2 adjustment/change in ventilator setting/other)
- Reason for termination of cerebral oximetry monitoring (cardio-pulmonal function has been stabilised/extubation/ infant exceeded 28 days after birth/infant deceased/other)
- Which oximeter device did you use to monitor the infant (INVOS/NIRO/Fore-Sight/Sensmart/O3 or Masiomo/Egos/ Oxyprem 1.4/Oxyprem NOAH/other)

Data to be reported at end of monitoring for infants in the usual care group

- Cerebral oximetry monitoring despite being in usual care group (yes/no)
  If yes:
  - Reason why the infant underwent cerebral oximetry monitoring despite being in the usual care group (free text)
  If yes:
  - Cerebral oxygenation values visible for clinical staff (yes/no)

Infants randomised with prior informed consent

- Withdrawal of consent from parents and reason if ‘yes’ (yes/no)
- Permission to use future clinical data (yes/no)

Infants randomised with opt-out

- Opt-out by parents after randomisation (yes/no)
- Permission to use future clinical data (yes/no)

Infants randomised with deferred consent

- Decline of continuing in the trial by parents and reason if ‘yes’ (yes/no)
- Permission to use future data and/or data up until withdrawal (yes or no)

Serious adverse reactions for infants randomised to the cerebral oximetry group
All serious adverse reactions must be registered in the eCRF when cerebral oximetry monitoring is terminated. It is also possible to register serious adverse reactions immediately after they occur. All registrations should be followed by a free text description of the reaction.

- Severe skin damage
- Critical displacement of endotracheal tube
- Critical displacement of endovascular line
- Mismanagement while trying to improve respiratory status
- Mismanagement while trying to improve cardiovascular status
- Mismanagement while trying to improve oxygen transport

Data to be reported at 90 days from randomisation

- Did the infant die within 90 days of randomisation? (yes/no, if 'yes' also cause and date of death)
- Did the infant suffer from any major malformation or congenital disease (yes/no)
- Beyond the first episode of invasive mechanical ventilation, was the neonate reintubated and mechanically ventilated? (yes/no)
- Did the neonate receive treatment for patent ductus arteriosus (medical or surgical)? (yes/no)
- What was the last registered weight of the infant before follow-up? (grams)
- Date of last weighing? (dd-mm-yyyy)
- Hospital-free days within 90 days of randomisation based on review of health care records (see primary outcome log, days)
- Additional days in hospital (not reported in clinical records) based on perental information (see primary outcome log, days)
- Total number of hospital-free days based on clinical records and parental information (see primary outcome log, days)
- Did the infant develop bronchopulmonary dysplasia grade 2 or higher? (yes/no)
- Did the neonate undergo MRI, cerebral ultrasound or CT scan at any time up until follow-up? (MRI, cerebral ultrasound, CT or no brain imaging)
- Did the neonat have a seizure that was treated with anti-seizure drug(s) (yes/no)
  If yes:
  - Was the seizure confirmed by EEG? (yes/no)
  - Was the seizure treated with more than one anti-epileptic drug? (yes/no)
  - Did the seizure recur within three days? (yes/no)
- Did the infant receive vasoactive drugs or hydrocortisone due to arterial hypotension? (yes/no)
- Did the infant receive vasoactive drugs or hydrocortisone due to signs of compromised systemic perfusion (yes/no)
- Did the infant undergo ECMO? (yes/no)
- Did the infant suffer from NEC Bells stage ≥2 or spontaneous intestinal perforation grade ≥3 (yes/no)

- Did the neonate undergo renal replacement therapy? (yes/no)
- Did the neonate suffer from suspected or confirmed late-onset sepsis (yes/no)
- Did the neonate suffer from confirmed or suspected invasive mechanical ventilation (endotracheal or tracheostomy)-related infection? (yes/no)
- Days in invasive mechanical ventilation (days)
- Was the neonate discharged home before follow-up? (yes/no)

List of possible brain injury imaging diagnoses (from Appendix B in the protocol)

- Peri-intraventricular hemorrhage (grade ≥2): Hemorrhage occupying less than 50% of the ventricle volume.
- Periventricular haemorrhagic (venous) infarction.
- Post-haemorrhagic ventricular dilatation: ventricular dilatation with ventricular index > 4mm above the 97th percentile or anterior horn with >6 mm or need of CSF removal (drain, shunt, reservoir, lumbal puncture).
- Periventricular leukomalacia (grade 2) (CUs diagnosis): Transient periventricular echodensities evolving into small, localized frontal-parietal cysts or persistent diffuse echodensities.
- Extensive punctate white matter injury (MRI diagnosis).
- Perinatal ischemic stroke.
- Acute HI brain damage:
    - (CU diagnosis): i) brain swelling; ii) bilateral-symmetric basal ganglia-thalamic injury or focal (asymmetric) hyperechoic areas; iii) laminar cortical necrosis; iv) periventricular and/or subcortical white matter injury
    - (MRI diagnosis): i) Central and/or peri-rolandic gray matter damage; ii) Hypoxic-ischemic injury in watershead areas.
- Cerebellar injury (ischemic-haemorrhagic) involving vermis or >1/3 of hemisphere.
- Big extra-axial bleeding or parenchymal bleeding/contusion with/without midline shift.
- Other: imaging findings related to CNS acquired infection.

Data to be reported for renal ancillary study

- Did the infant die before discharge (at a maximum of 90 days after randomisation)? (yes/no)
- Did the infant undergo renal replacement therapy at any time point up until discharge (at a maximum of 90 days after randomisation)? (yes/no)

Serum creatinine values from birth up until discharge

- Date of blood sample (dd-mm-yyyy)
- Serum creatinine value in mg/dL
- Serum creatinine value in µmol/L

If no sample is taken:

- No creatinine samples taken (checkbox)

Data to be reported for hypocapnia ancillary study

- Type of sample (Arterial/venous/capillary)
- Sample date (dd-mm-yyyy)
- Sample time (HH:mm)
- pCO_2
- pCO_2 unit (mmHg/kPa)
- $rStO_2$ at time of blood gas draw (%)
- Change in minute volume (yes/no)
- $rStO_2$ 15 minutes after change (%)
- Preductal SpO_2 (%)
- $tcpCO_2$
- $tcpCO_2$ unit (mmHg/kPa)
- FiO_2 (%)
- MAP (mmHg)
- Hypocapnia data file (upload)

  If no sample is taken:
  - No blood gas data (checkbox)

Data to be reported for cardiovascular ancillary study

- Did the infant receive any cardiovascular intervention before randomisation? (yes/no)

  If no:
  - Occurrence of any cardiovascular intervention within 72 hours from randomisation? (yes/no)

    If yes (multiple interventions can be added):
    - Date of cardiovascular intervention (DD-MM-YYYY)
    - Time of cardiovascular intervention (HH:MM)
    - Type of intervention (Fluid bolus administration / Vasoactive medications / Corticosteoroids)
    - Indication for initiation of cardiovascular support (Compromised circulation indicated by clinical parameters / Compromised circulation as assessed by echocardiography / cNIRS values – if randomised to cerebral oximetry group)
    - Contribution of clinical parameters (1-5)
    - Contribution of echocardiography findings (1-5)
    - Contribution of cNIRS values (1-5) – if randomised to cerebral oximetry group