SafeBoosC-III trial
(information for NICUs)

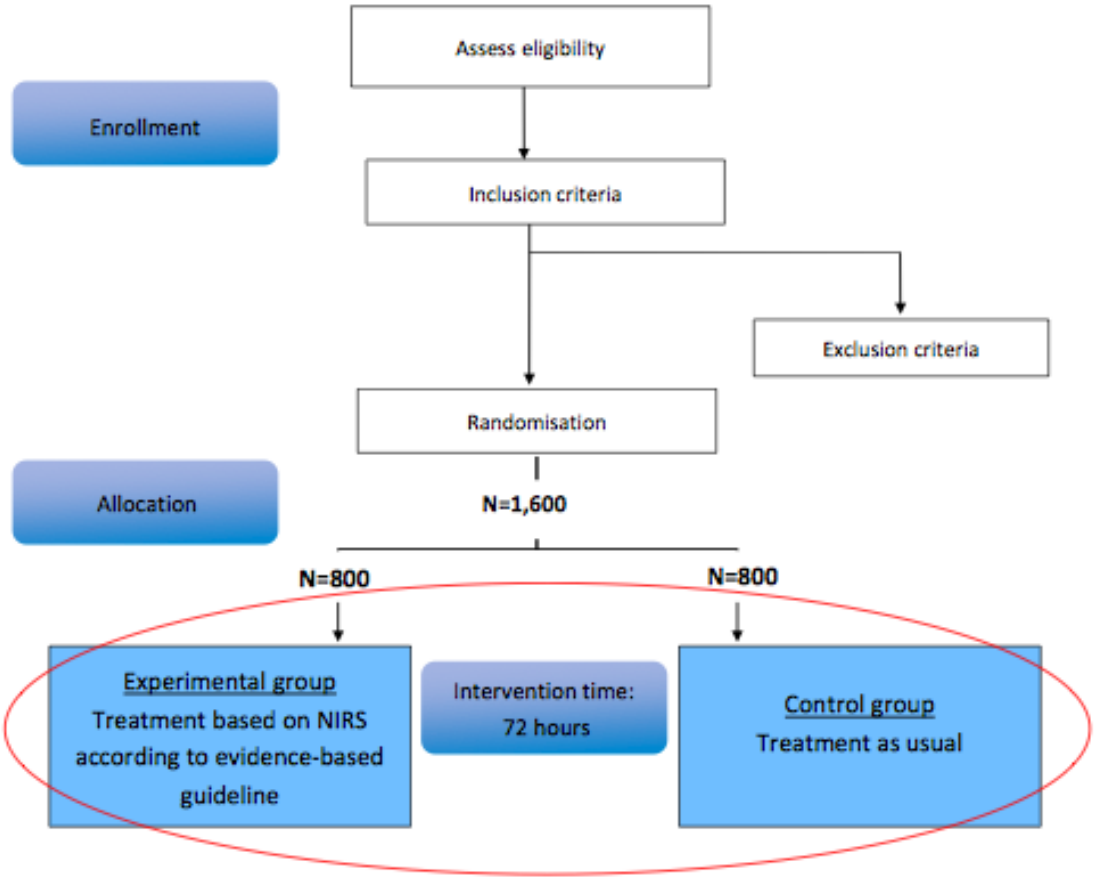
Purpose: Examine the benefit and harms of cerebral oximetry by NIRS combined with an evidence-based treatment guideline during the first 72 hours of life in extremely preterm infants

Primary outcome: Death or survival with severe brain injury at 36 weeks postmenstrual age or discharge home.

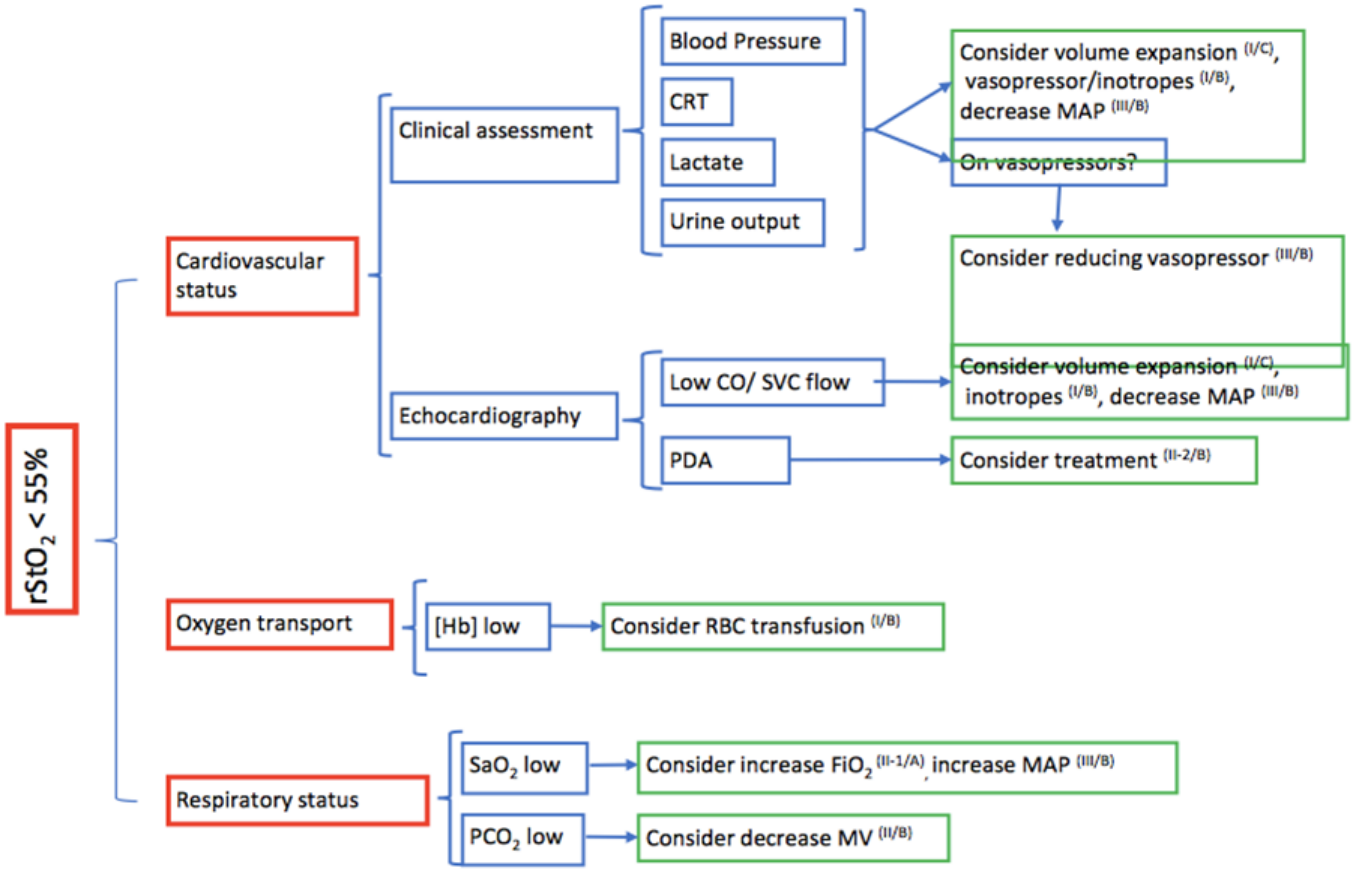
Explorative outcomes: Major neonatal morbidities count, NEC, BPD, ROP, Sepsis

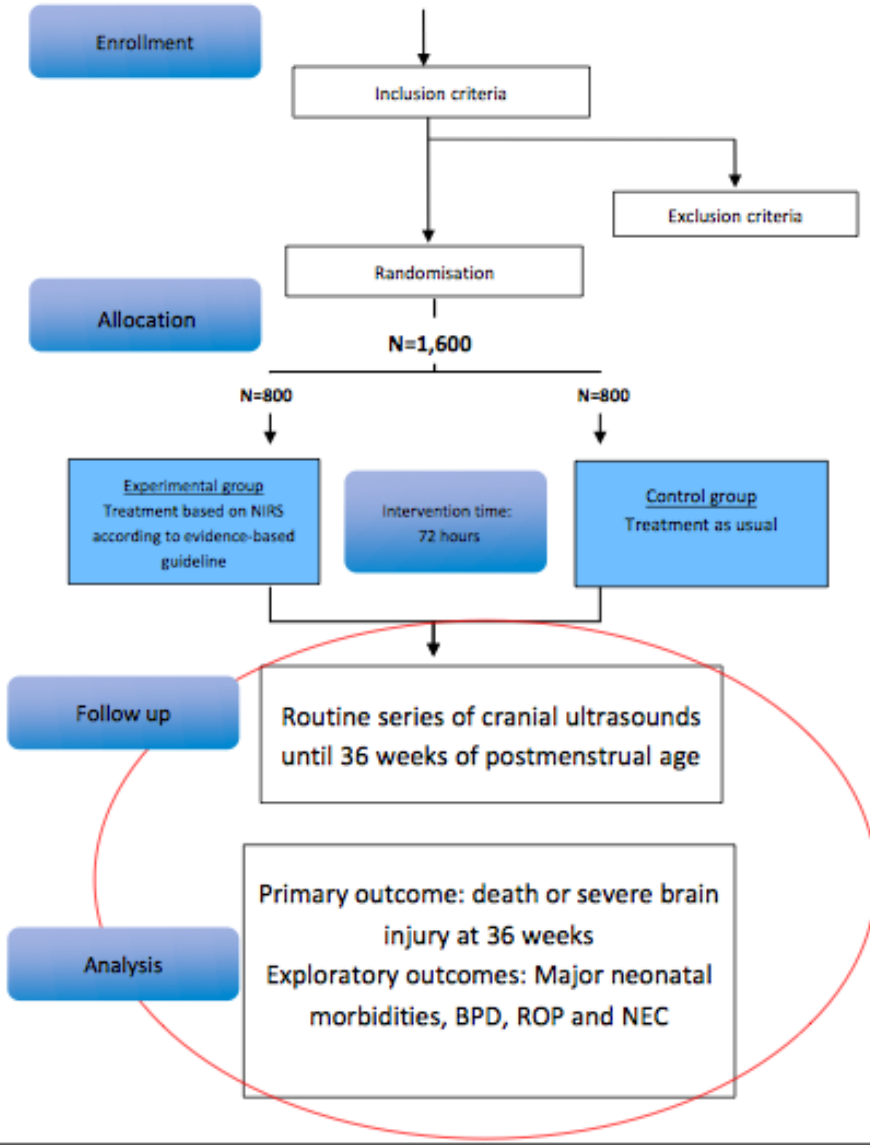
26-April-2019 / Gorm Greisen and Mathias Lühr Hansen

SafeBoosC phase III trial



Treatment guideline




Enrollment
Inclusion criteria
Exclusion criteria
Randomisation
Allocation
N=1,600
N=800
N=800
Experimental group
Treatment based on NIRS according to evidence-based guideline
Intervention time: 72 hours
Control group
Treatment as usual
Follow up
Routine series of cranial ultrasounds until 36 weeks of postmenstrual age
Analysis
Primary outcome: death or severe brain injury at 36 weeks
Exploratory outcomes: Major neonatal morbidities, BPD, ROP and NEC

Organisation

Randomisation 1:1 to experimental group or treatment as usual within 3 hours after birth

N = 800 + 800 infants to detect a reduction of primary outcome from 34% to 26%

50 (or more) NICUs in 21 countries (or more)

National coordinators

NICU principal investigators

Clinical Trial Unit and coordinating investigator in Copenhagen

Ancillary studies

- Patients can take part in any other study or trial if there is no conflict of protocol
- Partners are encouraged to organise ancillary studies drawing on SafeBoosC-III data
- Ancillary studies must not compromise the main trial and be approved by the steering committee and usually published after the main results

Funding

Available for

- Trial management
- Clinical trial unit/randomisation/ data management/statistical analysis
- Web-based system for training/certification
- Hospitality for investigator meetings
- Monitors and sensors (see next slide for details)

Not available for

- Ethical committee/GCP/patient insurance
- Investigator or national coordinator efforts
- Travel to investigator meetings

Equipment support

Europe: Oxyprem

China: EnginMed

US: Masimo (FDA approved neonatal sensor in September)

Cerebral oximeters

- All cerebral oximeter/sensor combinations that are approved for clinical use in newborns can be used
- Specific intervention thresholds will be defined to compensate for differences in operation

Publication and authorship

Publication of primary outcome:

- Small writing group + detailed description of contributions
- Plan A: Authors:
  - one per NICU (at least 30 patients) order by number of infants
  - National coordinators
  - CTU statistician
  - Steering group
- Plan B: Collaborative author ‘The SafeboosC-III study group’

All other publications as approved by Trial Steering Committee

Tasks per patient

- Obtain parental consent and do web-based randomisation
- Perform cerebral oximetry until 72 hrs and implement treatment guideline in the experimental group
- Perform cranial ultrasound as per clinical routine
- Fill web-based eCRFs (at randomisation, 72 hrs of age and at 36 weeks or discharge home) for a minimal dataset
- Present patients files for GCP visits

Tasks for participating NICUs

- Remain in equipoise during trial
- Obtain ethical approval
- Organise GCP monitoring
- Sign collaboration agreement
- Let relevant clinical staff complete web-based training and certification
- Enroll first patient April 2019
- Enroll at least 30 infants in two years

External monitoring (GCP)

- Initiation visit and close-out visit
- All centres
  - Check of delegation and training log
  - Check of patient inclusion list
- All patients
  - Existence of clinical file and parental consent
  - Gestational age under 28 weeks PMA
  - Group allocation
  - Dead or alive at 36 weeks PMA

Internal trial monitoring

- Enrollment
- eCRF completeness
- Summary statistics accross treatment groups
- Web-based training certification rates

This is done monthly per NICU with feedback and published in anonymised form on www.safeboosc.eu

Time line - draft

June-2018: Expression of interest and national coordinators identified

Oct-2018: Final protocol available for translation and ethics approval

Nov-2018: Investigators meeting to decide 'go'

March-2019: Web-based training and certification system open

April-2019: Design paper and statistical analysis plan paper submitted

April-2019: First patient randomised

July-2021: Last patient 36 wks PCA

Oct-2021: Report of primary outcome submitted for publication