Summary of Investigator Meeting SafeBoosC III

8-9th of November 2018 at Bella Sky Conference Center in Copenhagen, Denmark

A summary of important discussions and a short outline of presentations held during the two-day meeting.

8th of November

Session 1 – Welcome and introduction to SafeBoosC

- Welcoming speech – Gorm Greisen
- SafeBoosC II – Simon Hyttel Sørensen
- SafeBoosC III, The Organization – Mathias Lühr Hansen
- 'Stand up and speak' – National coordinators

National coordinators stood up and gave a personal presentation, status on NICU recruitment and what they believe are the biggest challenges so far. One of the biggest challenges voiced was financial issues, especially regarding NIRS instruments and Good Clinical Practice. We have applied for funding to cover this through Medtronics and are still awaiting their response. Another challenge which was mentioned by several investigators, was how the trial might interfere with competing trials. Although none of these trials stand in direct correlation with SafeBoosC III nor do they have similar outcomes, it may be hard to get consent from parents for participation in several trials.

Some NICUs only have very few pre-term babies and it will therefore be a challenge to recruit the 30 babies in two years.

9th of November

Session 2 – The Protocol

- SafeBoosC III protocol – Monica Fumagalli, Petra Lemmers, Eugene Dempsey, Janus Christian Jakobsen, Adelina Pellicer, Mathias Lühr Hansen, Simon Hyttel-Sørensen, Jonathan Mintzer

The question was raised whether sepsis should be included as an exploratory outcome. The steering committee will go on with determining whether sepsis should be included.

It was also discussed whether it was a possibility for several NICU's in the same region to split the number of infants to recruit. It was concluded that a unit is a NICU at one hospital, because otherwise there would be too large of a variability between units. It is important to underline, that if the total of 30 infants are not enrolled, the already recruited infants will not be discarded from the trial.

An interim analysis will also be conducted, and that a Data Management and Safety Committee has been appointed.

Some NICUs do a cranial ultrasound within the first few hours of birth on premature born infants. It was mentioned, whether it would be an exclusion criterion if this ultrasound showed prenatal brain injury prior to randomization. After a good discussion, it was agreed on that this was not common practice and will not be an exclusion criterion.

The cranial ultrasound at 36 weeks GMA should also be blinded to prevent bias. As is the case for sepsis, this will be discussed in the steering committee.

NIRS instruments used in this trial are required to be approved for clinical use in the relevant country (CE marked in Europe or FDA in the US, China?). Some concern was pointed out regarding the sensitivities of the different instruments. Even though the different instruments have distinct sensitivities and thresholds, this will be accounted for by calibration in the blood-lipid phantom. Concern was expressed towards the heterogeneity amongst the centers and adherence to the NIRS treatment guideline.

In the event of twins eligible to be recruited to the trial, they are to be randomized together. If the NICU is short on NIRS instruments, the last twin should always be chosen for enrollment. Triplets and quadruplets are not to be enrolled in the trial.

The protocol will be published as well as the statistical analysis plan which will add to the credibility of the trial.

It was asked if anybody had yet used the 'final' protocol version that is available a www.safeboosc.eu for ethics approval. Nobody had. Therefore it was decided to modify the protocol within the coming two weeks after the decision of the steering committee on the issues of sepsis and blinding of cerebral ultrasound. Thereafter, changes will appear as formal amendment, that need to be sent to regulatory authorities. So these are to be kept at a minimum.

- Ethics and Consent – Gorm Greisen, Mathias Lühr Hansen

- Webbased training and certification course – Colin Peters, Snorre Rubin, Mathias Lühr Hansen

The outline of the Moodle-based dynamic learning system was presented. It was discussed how to design an e-learning training course as easy-accessible and efficient as possible. Nurses will not be completing as many modules as doctors, but doubt was expressed towards the participation rate of nurses in the course, because of their busy workday. This e-learning program needs to be designed to their convenience, so the trial achieves a completion rate as high as possible of the training program. The trial does not require a specific amount of staff to be certified through the e-learning program. Other alternatives to the e-learning program were discussed as well, but executive committee members are hopeful, that if the access to Moodle and the course is streamlined, it can permanently familiarize staff at NICUs to cerebral oxygenation monitoring, also for NIRS implementation in NICUs outside the SafeBoosC trial. The data collection and assessment from the e-learning course will also be published as an ancillary study.

GCP, Ancillary studies, economy and decisions

- GCP plan – Mathias Lühr Hansen

The trial requires one GCP person per center. This person must be GCP trained and not involved in the trial, including care of trial participants. If it could be of convenience for several units, it is warmly welcomed to use a national GCP person. After the meeting, investigators in Copenhagen will meet with GCP experts to finalize the monitoring plan.

- Ancillary studies – Mathias Lühr Hansen, Gorm Greisen

  Four ancillary studies were presented and more details regarding these can be found on the SafeBoosC website (safeboosc.eu)

- Economy – Gorm Greisen

  Funding has been applied for, and we are currently awaiting assessment from Medtronic and NovoNordisk Foundation.