Minutes from the SafeBoosC Steering Committee Meeting the 17th of March 2020, at 20:00

Apologies from: Saudamini Nesargi, Jonathan Mintzer, Monica Fumagalli, Hans Fuchs, Gerhard Pichler and Anne Marie Heuchan, Cornelia

Absent: Cheng, Ana, Olivier

Attendees: Ebru Ergenekom, Adelina Pellicer, Thomasz Szczapa, Christian Gluud, Gunnar Naulers, Gabriel Dimitriou, Siv Fredly, Simon Hyttel-Sørensen, Jakub Tkaczyk, Gene Dempsey, Gorm Greisen, Mathias Lühr Hansen, Marie Rasmussen

CoVid-19 and SafeBoosC III

We are aware that this could cause delay due to some hospitals putting research on hold during the outbreak. However, SafeBoosC III is resilient to delays due to the decentralised funding. Furthermore, the majority of the hospitals that are already randomising, have reported to us that the CoVid-19 outbreak have not yet affected enrolment. The only potential conflict could be the decentralised monitoring (local GCP), since the GCP person often needs to come to the ward in order to conduct the visit and this might not be permitted in all hospitals, and may be delayed to after the epidemic. With advice from Copenhagen Trial Unit, it is consensually agreed to conduct monitoring, whenever it is possible. Every site should report on the current situation, if they are obliged to postpone.

Status and progress of trial preparations from last meeting, by national coordinators

Currently, 32 sites are open for randomisation. At this time, randomisations rates are low, but we are confident that they will increase once the CoVid-19 pandemic has passed.

Adelina Pellicer - Spain

Ten sites are currently randomising, and three more sites are waiting to open-up for randomisation. Some delays are to be expected, due to not being able to meet in person.

Gunnar Naulaers - Belgium

Waiting for approval from central ethical committee. Funding has been approved. Contracts are pending. Hopeful to start mid-April or latest May, first in Leuven in order to get practical experience to allow guidance to others sites.

Gabriel Dimitriou - Greece

Three centres are randomising, and the fourth only need to complete the GCP initiation visit in order to start randomising as well. Most units are currently working with half the personnel, due to Covid-19 and they are furthermore facing some logistical problems regarding the randomisation and cUS follow-up on patients.

Siv Fredly - Norway

Both Norwegian sites have ethics approval and are working on the additional trial preparation tasks. In Olso, they cannot start randomising until another trial has been completed. Siv will contact Bergen to ask about progress.

Simon Hyttel-Sørensen – Denmark
Three centres are open for randomisation and a fourth is working on the final tasks. So far, only Copenhagen has randomised babies. Simon will contact PIs to ask if there are particular issues to be addressed.

Ebru Ergenekon – Turkey
Five centres are open for randomisation, and four of these have randomised babies.

Tomasz Szczapa - Poland
Eleven centres are expected to participate. Currently, only three are open for randomisation. Due to CoVid-19 they are running NICUs with only half of normal staff. However, it is not expected to affect randomisation nor monitoring.

Jakub Tkaczyk - Czech Republic
Two centres are participating, and one is randomising. The remaining centre still faces logistical problems, so expected start date is unknown. In the meantime, staff will be trained and the learning material will be translated into Czech so that a Czech version of the training program can be available online.

Gene Dempsey - Ireland
The University has shut down due to CoVid-19, so contracts are still pending. Copenhagen and Cork will have a bilateral agreement and then Cork will serve as national sponsor with contracts between individual departments. Will soon receive message on funding.

Austria – Mathias Hansen
One centre participating. They are only missing GCP visit to open up for randomisation.

China – Mathias Hansen
Three centres are open for randomisation and a few more are working on trial preparation tasks.

Italy – Mathias Hansen
Except for Milan whom are already randomising, the trial has been put on hold due to the CoVid-19 outbreak.

Portugal – Mathias Hansen
Three Portuguese centres are formally participating. However, only one has completed one of the SafeBoosC trial preparation tasks.

UK – Mathias Hansen
So far, two Scottish centres will be participating. Ethics approval, covering all of UK has been obtained. Anne Marie may reach out to a few additional UK centres if Glasgow Clinical Research Unit accepts, since ethics approval will cover. Both centres have started training and are working on the collaboration agreement.

US – Mathias Hansen
Still waiting for answer on the CPARF grant application, which will hopefully come in March. Ten hospitals are depending on this grant, in order to participate in the trial. An additional three hospitals will be participating despite no funding and are expected to start randomising within one month, expect for one centre who have put all research on hold due to CoVid-19

Ancillary studies, discussion and vote
Enough members (n=12, > 50%) of the steering committee (n=21) are present to constitute a quorum.

General movement assessment ancillary study by Gerhard
Questions were raised regarding blinding, since in Spain it will be the neonatologists that do the assessment. But if the baby is naked and the video is pseudo-anonymised, blinding is possible. The need and timing for parental consent was discussed. In Denmark, consent is not required for this study, since it will use routinely collected health care data. It will require an authority permission though. This may differ in other countries. Finally, local calculation of the two-by-two statistics is envisioned with transfer of the results to Graz as input to a meta-analysis which will yield the common result. This is planned to avoid the need for a separate set of data processing agreements.
All members (12/12) voted in favour of Gerhard to include the requested details to the protocol. The plan is to circulate the final version of the protocol by mail to the steering committee for approval. The protocol will be placed on the SafeBoosC website and the study must be registered at clinicaltrials.gov (this will be a general requirement for ancillary studies).

Renal tissue oxygenation ancillary study by Tomasz
It was debated whether consent for the renal StO2 ancillary study should be included in the consent for the SafeBoosC III trial. It is suggested that the consent form could contain a separate tickbox. It is critical that the renal StO2 is not available to clinical staff. Tomasz thoroughly explained by powerpoint how this is achieved.
So far, this ancillary study is a Polish study, but it is open to centres from other countries. The steering committee argued that the protocol needs to include a statistical analysis plan, including a power calculation based on a minimal clinical important difference, as well as precisely defined outcomes. All members (12/12) voted in favour of Tomasz to include the requested details to the protocol, before circulation by mail for approval.

SafeBoosC III 2-year follow-up study
Copenhagen proposed to take the lead on this. Marie will apply for a MD/PhD study program at Copenhagen University and we are confident that we can find funding for her. Marie is already well into the trial and started the work on the protocol. We will be in touch with investigators shortly, to get information on regarding which neurodevelopmental follow-up assessments that are routinely performed at the participating sites, as well as to hear if you would be interested in participating in the follow-up study.
All the present members of the steering committee voted in favour of Copenhagen taking the lead in this project.

Case from Zürich, randomisation before birth – what is our opinion?
The steering committee agrees that it is no problem to randomise a baby before it is born, if the decision to provide full life support has been taken, and the risk is very small that the baby will die during delivery or change that decision.

The meeting ended at 21:45.