Minutes from the SafeBoosC-III steering committee meeting the 22nd of September 2020

Attendees: Hans Fuchs, Gunnar Naulers, Jakub Tzackub, Christian Gluud, Ebru Ergenekon, Adelina Pellicer, Cornelia Hagmann, Saudamini Nesargi, Siv Fredly, Tomasz Szczapa, Janus Jakobsen, Monica Fumagalli, Gene Dempsey, Gabriel Dimitriou, Gorm Greisen, Mathias Lühr Hansen, Marie Rasmussen

Apologies: Gerhard Pichler, Jonathan Mintzer, Simon Hyttel-Sørensen

Absent: Guoqiang Cheng, Anne Marie Heuchan, Ana Vilan

Trial status update from Copenhagen
Currently, 54 centres are open for randomisation. Since the last meeting in July, six hospitals have opened for randomisation. It is expected that, within the next six months, a total of 65 centres will be open for randomisation. As of the 18th of September, 465 babies have been randomised, and the randomisation rate is increasing. If we continue at the current randomisation rate, we will reach the sample size by March of 2022. However, as we expect ten new hospitals to open for randomisation, it is believed that we will reach the sample size by the end of 2021. Gorm emphasizes that the same trend was seen in SafeBoosC-II, where the randomisation rate increased towards the end of the trial. Some investigators raised a concern regarding the effects of a second COVID-19 wave on the randomisation rate.

Updates on trial execution, by national coordinators

Denmark – by Gorm (Simon Hyttel-Sørensen)
Rigshospitalet is recruiting smoothly, whereas the other three centers are including at a slower rate.

Germany – Hans Fuchs
Three babies have been randomised. No additional German centres are expected to participate in the trial.

Turkey – Ebru Ergenekon
Still not through the first wave of the COVID-19 pandemic and have seen a decrease in extremely preterm infants. Some principal investigators have been rotated to other sites, due to organisational changes caused by the pandemic, but are keen to proceed with randomisations on the new centre. They expect to be up and running at the new centre within a month.

Belgium - Gunnar Naulers
Five of the six centres are open for randomisation and three have already randomised babies. The last centre is expected to open for randomisation shortly.

Czech Republic - Jakub Tkaczyk
One centre is randomisation babies in a good tempo, while the other is still facing organisational changes and might not be able to start until Christmas.

Spain - Adelina Pellicer
Eleven centres are open for randomisation. However, some of the centres have a lower randomisation rates than expected. Adelina is concerned that some centres will not reach the 30 randomisations required for co-authorship. It is agreed that this issue shall be addressed at some point in the future.

Norway - Siv Fredly
The competing study has been delayed due to the pandemic. Hopeful to start after Christmas.

Poland - Tomasz Szczapa
Four centres are open for randomisation and three have randomised babies. An additional four centres are expected to be opened for randomisation within the next three months. Their preparations for the trial have been delayed due to shipment problems with OxyPrem devices. However, most centres have received their devices now.

Italy - Monica Fumagalli
Two centres are open for randomisation and one has already randomised. A third centre is progressing well with trial preparations and are expected to open for randomisations within the next months. The centre who have randomised babies, have had some experience with parents declining to participate in the trial, which could be due to the conduct of multiple trials in that centre.

Ireland - Gene Dempsey
Contracts are signed regarding the primary Irish site. They are hopeful to open for randomisation within the next weeks, and one more centre is expected to follow.

Switzerland - Cornelia Hagmann
All four Swiss centres are open for randomisation. Some sites have seen a declined rate of extreme prematurity and some have temporarily stopped the conduct of randomised clinical trials, due to the pandemic, but the situation is normalising.

Greece - Gabriel Dimitrou
All for Greece centres are open for randomisation and they have all randomised.

India - Saudamini Nesgari
Has randomised the first infant. An additional Indian site is negotiating the contract and insurance payment locally. If they can meet terms with the centre director, they are expected to participate in the trial as well.

China – by Mathias (Guoqiang Cheng)
Four centres have randomised babies. An additional four centres are open for randomisation as well.

Portugal – by Mathias (Ana Vilan)
Uncertain if any centres will participate in the trial.

United States – by Mathias (Jonathan Mintzer)
Two centres have just opened and randomised four babies. Two more are expected to open up within the next two months.

Ukraine and France are not expected to participate in the trial

When will we close the door for new centres and how
It was discussed when the doors should close for new centres wanting to enter the trial. As for now, too many centres are currently preparing to open for randomisation and the steering committee agrees that for now, there will be no decision on when and how the doors shall close. The matter will be discussed again at the next steering committee meeting in two months.

Decision on the design of the SafeBoosC-III follow-up study

1) **The degree of follow up data** - *more or less work for the PI? Should we collect clinical information from other sources and/or parental questionnaires (if not normally implemented) to supplement the information available from routine follow-up*?
   There was a positive attitude towards the distribution of parental questionnaires in addition to routine follow-up data. The questionnaires discussed were the Ages and Stages Questionnaire (commercialized) and PARCA-R (open access). Centrally we will work on a pragmatic solution on how distribute this in 17 different languages, which will be presented at the next meeting. A possibility could be online.

2) **Blinding** - *should we encourage the PI to design and implement measures as necessary and possible, to minimize the risk that the professionals that undertake clinical assessment of SafeBoosC participants are aware of their group assignment?*
   The steering committee discussed, that the chance of the clinician conducting the assessments and furthermore being biased by the child's allocation group in the SafeBoosC-III trial is highly unlikely. In some centres, the clinicians involved in routine follow-up are not implicated in ICU care. Janus from CTU emphasizes that clinicians should merely be instructed to refrain from looking at the child's group allocation, or instructed in not to look at the clinical records of the child, until after conducting the formal assessment.

3) **Number of children to follow-up to obtain co-authorship** - *how to obtain minimal loss to follow-up without excluding any NICUs*
   The steering committee agrees that a follow-up percentage of 75% of surviving children is required to obtain co-authorship. This can be changed later on by the steering committee.