Minutes from SafeBoosC III Steering Committee Meeting - 20th of July 2020

Attendees: Hans Fuchs, Gerhard Pichler, Jonathan Mintzer, Ebru Ergenekon, Saudamini Nesargi, Janus Jakobsen, Monica Fumagalli, Tomasz Szczapa, Simon Hyttel-Sørensen, Gabriel Dimitriou, Ana Vilan, Mathias Lühr Hansen, Gorm Greisen, Marie Rasmussen

Apologies: Gunnar Naulaers, Cornelia Hagmann, Gene Dempsey, Adelina Pellicer

Missing: Guoqiang Cheng, Siv Fredly

Trial status update from Copenhagen
Currently, 48 centres are open for randomisation while an additional 31 centres are actively preparing to randomise. Although the number of centres opened for randomisation has increased by 23% since the last steering comitte meeting, the randomisation rate has decreased slightly. In response to this, several investigators report that the rate of extremely preterm infants is still low in their respective centres, most likely as a result of the COVID-19 outbreak. Thus, there is confidence that the rate will increase shortly and that the pandemic, all things considered, has had a minor impact on the SafeBoosC III trial.

News on trial preparations, by national coordinators

Gerhard Pichler – Austria
Graz has randomised the first baby recently. Graz will also be the only Austrian center participating in the trial.

Jonathan Mintzer – United States
Currently, one center is open for randomisation and an additional two are expected to open within a month. The grant application for CPARFF 2020, supposed to cover an additional eight US centres has been postponed to 2021, meaning that the participation of these eight centres is unlikely.

Hans Fusch – Germany
Freiburg has been open for randomisation for three weeks and there has been no eligible babies. Will start e-learning once they have randomised the first baby

Jakub Tzackub – Czech Republic
One center is randomising and will most likely be the only Czech center, as the other is facing significant organisational difficulties

Monica Fumagalli – Italy
One center is open for randomisation, while two more centers are very close to be able to start. Unfortunately, one center recently declined to participate in the study due to the lack of insurance coverage.

Saudamini Nesgari – India
The only participating Indian centre is open for randomisation, but since the prematurity have dropped significantly during COVID, no babies have been randomised yet.

Simon Hyttel-Sørensen – Denmark
All four sites are open for randomisation and all but one have randomised babies.

Gabriel Dimitrou – Greece
Four centers are open for randomisation and all four have randomised babies.

Ana Vilan – Portugal
One center is expected to open for randomisation in mid-august. Staff is working on the e-learning. It seems like only one portugise centre will participate.

Ebru Ergenekom - Turkey
Five centers are open for randomisation and all five have randomised babies.

Tomasz Szczapa - Poland
Four centers are open for randomisation whereof three have randomised babies. The last center is waiting for eligible babies. An additional seven centres are actively preparing for the trial, however it is unlikely that all seven will end up randomising babies.

Ireland – Gene (by Gorm)
The three centres in Ireland are still in the preparation phase, unsure when they will be able to start. However, they will start the trial despite the lack of funding.

When will we close the doors for new hospitals and how?
Janus from CTU explains how few events of the primary outcome in individual centres may result in statistical problems. Therefore, it is better to have fewer centres with a nigh number of events (at least 5, optimal 10) instead of more centres with fewer events. 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.

Practical issues with monitoring the smallest babies?
There have recently been two situations in Poland and one in Spain, where they were not able to get a signal with the Oxyprem sensor, when monitoring 23- and 27-week babies, due to small head circumference. In Poland, the babies were not randomised due to this issue and in Spain, the baby was randomised to the experimental group but the staff gave up on monitoring.
OxyPrem has recently sent a bending aid, which enhances the curvature allowing better contact between the sensor and the head, which Gorm has had good experience with. Investigators from other countries also share their experience with getting a signal on the smallest babies and it seems to be a problem related specifically to the Oxyprem sensor.

After discussion it was agreed in the steering group that it is up to the individual doctor whether they will randomise a baby if they suspect that it will difficult due to small head circumference. As an alternative, the baby can be randomised, and if in the experimental group, monitored as well as possible, potentially by hand held ‘spot’-measurements when clinically indicated. The argument is that this is a pragmatic trial, testing the effect of the intervention in a real-world situation and such difficulties is part of the usage of NIRS monitoring and thus, it should be dealt with as decided by individual doctors. The protocol will not be changed.

Issue with registering the GMA ancillary study on clinicaltrials.gov – what to do?
It was concluded that Gerhards GMA study should be registered on clinicaltrials.gov as an RCT study, and that it should be described – in the title as well as the text – that the study is based on the two SafeBoosC cohorts as randomised and will analyse the effect of the intervention on a separate outcome, not described in the protocol, in a subset of NICUs.
No further business.