Minutes from the SafeBoosC consortium steering committee meeting 3rd of January 2024 at 21:00

Attendees: Tomasz Szczapa, Jakub Tcakzub, Janus Jakobsen, Simon Hyttel-Sørensen, Eugene Dempsey, Saudamini Nesargi, Gunnar Naulaers, Adelina Pellicer, Christian Gluud, Siv Fredly, Anne Marie Heuchan, Gabriel Dimitriou, Hans Fuchs, Marie Rasmussen, Mathias Lühr Hansen, Gorm Greisen.
From CTU: Markus Harboe Olsen, Caroline Kamp Jørgensen

Apologies: Jonathan Mintzer, Ebru Ergenekon, Monica Fumagalli, Gerhard Pichler

Absent: Guoqiang Cheng, Cornelia Hagmann

SafeBoosC-III follow up study

The last child will turn two years of corrected age in April 2024 and data entries will close 6 months after this (Oct 2024). We have seen a slight decrease in data completions, which is probably due to 17 centers who have not started the follow up study yet, but have eligible infants. We went through all 17 centers and discussed possibilities with the national coordinators. It has been a challenge to establish contact with the 6 Chinese centers. There has only been sparse contact with the national coordinator. All have surpassed 6 months since the first child turned 2 years of corrected age. We know from previously that children are not routinely followed up in China. To limit missing data, it is proposed to exclude the Chinese centers. Enough members of the steering committee were present (>12) to constitute a quorum. This was unanimously approved.

Marie presents the CogniTOT ancillary study in Denmark which will validate the app in the SafeBoosC population, a population between 28-32 weeks gestational age and healthy term born controls. We will also correlate the scores to PARCA-R and ASQ scores.

Until now, only data completeness has been checked monthly. We will now work out the procedures for central check of data quality (consistency) so work for all investigators is anticipated for checking and correcting suspect data. Our aim is to finish data cleaning shortly after the last data entry and locking the database. The plan is also to work-out a precise and a statistical analysis plan including simulations on loss to follow up. Hopefully, this will allow us to have the final results of the study before Christmas 2024.

Marie, however, is still not funded for her last year, and plans may have to be changed accordingly.

SafeBoosC-IIIv

CTU has received 540k euros to cover the central costs for IIIv, including trial management, data management, developing of data systems, conducting statistical analyse for a trial with a 90-day primary outcome. The proposed primary outcome is hospital free days within 90 days from randomisation. In total, 1610 participants must be randomised to achieve sufficient statistical power to demonstrate a 5% relative risk reduction in mortality and a 3-day increase in hospital free days (based on simulations on a national Danish dataset). Janus explains that this outcome is a frequently used outcome in intensive care trials. The 90-day

outcome is seen as the first step in a two/three step ‘rocket’, and CTU will continue to seek funds to executethe already published protocol (https://doi.org/10.1186/s13063-023-07699-x.)

Janus emphasizes the importance of the current national coordinators participating actively, as CTU does not have any neonatologists on staff.

Gabriel is concerned that the primary effect measure will be difficult to interpret and that the group is too heterogeneous. Janus states that the sample size analysis is based on simulations of data from Danish children over a 10-year period. Saudamini asks if all hospitalizations including surgeries etc will apply for the 90-day period, to which Janus answers yes. It is asked if the surgical children with malformations will be randomized separately. Gorm states that this is not a stratification variable, rather it is prematurity. Too many stratifications in the randomisation will present statistical challenges. Tomasz asks what happens to the sample size if we obtain money for a two year follow up which requires 3000 participants to achieve sufficient statistical power. Janus replies that if we get this money we will continue with randomisations until we reach 3000 participants. It is also pointed out that the consent for the 2-year follow up must be included in the randomisation form. There is a concern that it may be hard to include enough moderate to late preterm children, as many are treated with less invasive surfactant treatment, so less and less children in this population are ventilated. Mathias says that OxyPrem has developed a new sensor, which is smaller and expect a CE marking at the end of 2024. They wish to support the centers who need sensors. Mathias has a list of appr. 80 centers, incl the SafeBoosC-III centers, who have reached out and wish to participate. China and Turkey have withdrawn.

There is a discussion on whether we should aim for a central collaboration with the industry, but this idea is turned down as industry may have different interests regarding this trial and it is agreed negotiations may delay the initiation of the trial. CTU will reach out to the industry to inform of our plans and provide contacts information on principal investigators since industry and dealers are interested in direct contact with potential customers. Meanwhile all centers who wish to participate in the trial are encouraged to seek out local funding opportunities.

Janus states that the goal is for randomization to start is at the end of 2024.

All present national coordinators wish to participate as national coordinators in the SafeBoosC-IIIv trial and all are positive towards pushing the trial forward.

No further business, meeting ended at 22:25