

SafeBoosC-III newsletter January 2022

Dear investigators

Welcome to the January 2022 issue of the SafeBoosC-III newsletter.

Investigator meeting in Copenhagen 19-20 of May 2022

The next SafeBoosC Investigator Meeting was planned from 24-25 of March 2022. However, due to the present COVID-19 situation, we had to reconsider the plans.

On the steering group meeting 24th of January, the possibilities were discussed, and the steering group agreed that the meeting should be postponed until May.

Therefore, the next SafeBoosC Investigator Meeting will take place in Copenhagen, 19-20 of May 2022. Since the statistical analyses will just have been completed by then, the session on Thursday night will be an “unblinding session”, where the trial results will be revealed.

Additional information has been sent out by e-mail to investigators, and more will follow soon, including an agenda.

Recruitment completed in December

On the 16th of December 2021, the last participants were randomised. Since the last randomisation was a “twins randomisation”, the sample size ended up being 1601 instead of 1600. The sample size was recruited from 70 centres across Europe, US, India and China.

A full overview of randomisations across all centres can be seen in table 1 (see page 4 and 5).

Plan for completion of SafeBoosC-III has been initiated

With recruitment completed, we now have an important job - to complete data entries, identify random and systemic errors in the entered data and complete all GCP reports. Until this is completed, the statistical analyses cannot be initiated, and the manuscript cannot be written and submitted for publication in The New England Journal of Medicine.

The completion process is fully described in the SOP “Completion of SafeBoosC-III and submission of manuscript”, which is available on safeboosc.eu:

<https://www.rigshospitalet.dk/english/departments/juliane-marie-centre/department-of-neonatology/research/SafeboosC-III/Documents/sop-completion-of-safeboosc-iii.pdf>

The SOP also includes an expected timeline, with important deadlines and tasks for investigators (planning GCP visits, time for data entry etc). Therefore, please read it carefully. We will do our utmost to respect the stated deadlines in the SOP.

Secondary publications

All principal investigators are allowed to plan and conduct secondary studies and subsequent publications based on SafeBoosC-III trial data. However, the study must be approved by the steering committee 'up-front'. If a single or a group of principal investigators, or members of the steering committee intend to do so, a description of the study must be sent to mathias.luehr.hansen@regionh.dk before 17th of March 2022.

The investigator(s) shall then present the study at the online meeting on 24th of March (link has been sent by e-mail) for discussion. After the investigator meeting, the steering committee will discuss the suggested studies and develop and decide on a 'secondary study and publication plan'.

More details can be found in the SOP "Secondary publications in SafeBoosC-III", which is available on safeboosc.eu:

<https://www.rigshospitalet.dk/english/departments/juliane-marie-centre/department-of-neonatology/research/SafeboosC-III/Documents/sops/sop-secondary-publications-240122.pdf>

Status on data completion

As we have initiated the trial completion phase, data completion monitoring will be conducted very 14th day. All reports are available on safeboosc.eu:

<https://www.rigshospitalet.dk/english/departments/juliane-marie-centre/department-of-neonatology/research/SafeboosC-III/Documents/safeboosc-iii-data-completion-report-230122.pdf>

For all data entry forms, data completion is increasing, when compared to the report from two weeks ago (data completion increase in parentheses).

- End of monitoring form: 99% (+1%)
- SARs form: 97% (+1%)
- Follow-up form: 99% (+1%)
- Blinded follow-up form: 94% (+3%)

Investigators with missing data entries have been contacted and urged to complete data entries.

SafeBoosC-III Follow-up

Six centers have participants that have reached two years of corrected age, and four of these have started completing data entries in OpenClinica. A total of 15 participants have had follow up data entered in OpenClinica, and 10 families have completed the parental questionnaire.

So far, the parental questionnaire is available in six different languages (English, Danish, Spanish, Czech, Italian and Turkish) with more translations to come. Some centers may experience that ethics committees' rule, that additional consent from families should be sought for the use of clinical data for the SafeBoosC-III follow up study. This may pose an extra challenge and investigators are therefore welcome to contact Marie, who can help manage this workflow.

SafeBoosC-IIIv

Unfortunately, we did not receive the grant from the Novo Nordisk Foundation. We are planning to continue to seek funding and expect an application to be strengthened after the result from the SafeBoosC-III trial is published. In the meantime, we are working on the design paper and await the decision from the ethics committee in Denmark regarding the trial protocol.

Minutes from the 16th steering group meeting

The latest steering committee meeting was held online through Zoom on the 24th of January. Please find the minutes, as well as minutes from all previous meetings on safeboosc.eu:

<https://www.rigshospitalet.dk/english/departments/juliane-marie-centre/department-of-neonatology/research/SafeboosC-III/Sider/newsletters.aspx>

Thank you for your time,
Gorm, Marie, Maria and Mathias

Table 1. Randomisations across participant centres

| Country | Centre | Randomised |
|-----------------------|---|-------------------|
| Austria | University Hospital Graz, Graz | 21 |
| Belgium | University Hospital Leuven, Leuven | 32 |
| Belgium | AZ St-Jan Bruges, Bruges | 14 |
| Belgium | Grand Hospital de Charleroi, Charleroi | 19 |
| Belgium | Tivoli Hospital, La Louviere | 19 |
| Belgium | Clinique CHC Montlegia, Liège | 24 |
| Switzerland | University Hospital Zürich, Zürich | 37 |
| Switzerland | Children's Hospital Lucerne, Lucerne | 44 |
| Switzerland | Children's University Hospital of Geneva, Geneva | 11 |
| Switzerland | University Hospital Center of Lausanne, Vaud | 23 |
| China | Children's Hospital of Zhejiang, Hangzhou | 6 |
| China | Children's Hospital of Fudan University, Shanghai | 35 |
| China | Hainan Women and Children's Medical Center | 5 |
| China | Guangzhou Women and Children's Medical Center, Guangzhou | 2 |
| China | Longgang Distict Central Hospital, Shenzen | 10 |
| China | Xiamen Children's Hospital, Xiamen | 4 |
| China | The People's Hospital of Dehong, Dehong | 3 |
| China | Maternal and Child Health Care Hospital, Quangxi | 7 |
| Czech Republic | The Institute for the Care of Mother and Child, Prague | 66 |
| Czech Republic | University Hospital Motol, Prague | 10 |
| Germany | Medical Center University of Freiburg, Freiburg | 16 |
| Denmark | Copenhagen University Hospital - Rigshospitalet, Copenhagen | 106 |
| Denmark | Aalborg University Hospital, Aalborg | 21 |
| Denmark | Aarhus University Hospital, Aarhus | 22 |
| Denmark | Odense University Hospital, Odense | 12 |
| Spain | La Paz University Hospital, Madrid | 78 |
| Spain | Hospital Clínic-Maternitat, Barcelona | 59 |
| Spain | 12 de Octubre University Hospital, Madrid | 73 |
| Spain | Hospital Sant Joan de Deu, Barcelona | 32 |
| Spain | Puerta del Mar University Hospital, Cádiz | 22 |
| Spain | Hospital Clinico San Carlos - IdISSC, Madrid | 36 |
| Spain | Marques de Valdecilla University Hospital, Santander | 23 |
| Spain | Virgen de Las Nieves University Hospital, Granada | 14 |
| Spain | Hospital Universitario de Tarragona Juan XXIII, Tarragona | 18 |
| Spain | Miguel Servet University Hospital. Zaragoza | 1 |
| Spain | University Hospital Cruces, Barakaldo, Spain | 4 |
| Greece | “Alexandra” University and State Maternity Hospital, Athens | 16 |
| Greece | Ippokrateion General Hospital of Thessaloniki, Thessaloniki | 40 |
| Greece | University of Patras General Hospital, Patras | 13 |
| Greece | University Hospital of Heraklion, Heraklion | 10 |
| Ireland | Cork University Hospital, Cork | 22 |
| Ireland | The Rotunda Hospital, Dublin | 19 |

| Country | Centre | Randomised |
|----------------|--|-------------|
| Ireland | Coombe Women and Infant University Hospital, Dublin | 18 |
| Ireland | National Maternity Hospital, Holles Street, Dublin | 19 |
| India | St John's Medical College, Karnataka, India | 5 |
| Italy | Ospedale S.Anna - Città della Salute e della Scienza di Torino | 11 |
| Italy | Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico Milan, Milano | 45 |
| Italy | "Filippo Del Ponte" Hospital, Varese | 12 |
| Italy | Fondazione Policlinico Universitario A. Gemelli IRCCS – Rome, | 15 |
| Norway | Oslo University Hospital, Oslo | 36 |
| Poland | Centrum Medyczne "Ujastek" Sp. z o.o., Krakow | 37 |
| Poland | Medical University in Wroclaw, Wroclaw | 1 |
| Poland | Specialist Hospital No.2, Bytom | 8 |
| Poland | Poznan University of Medical Sciences, Poznan | 34 |
| Poland | Collegium Medicum in Bydgoszcz Nicolaus Copernicus University in Torun, Bydgoszcz | 3 |
| Poland | Warsaw University of Medical Sciences, Warsaw | 9 |
| Poland | Jagiellonian University Hospital, Krakow | 20 |
| Poland | Centre of Postgraduate Medical Education, Warsaw | 4 |
| Turkey | Gazi University Hospital, Ankara | 17 |
| Turkey | Marmara University Research and Education Hospital, Istanbul | 33 |
| Turkey | Bursa Uludag University Hospital, Bursa | 44 |
| Turkey | Kanuni Sultan Suleyman Training and Research Hospital, İstanbul, Turkey | 11 |
| Turkey | Bilkent Integrated Health Care Campus, Ankara City Hospital and Maternity Hospital, Ankara | 37 |
| Turkey | Basaksehir Cam and Sakura City Hospital, Istanbul | 13 |
| United Kingdom | Royal Hospital for Children Glasgow, Glasgow | 21 |
| United Kingdom | University Hospital Wishaw, Wishaw | 11 |
| United States | Loma Linda University Children's Hospital, Loma Linda | 38 |
| United States | University of Utah Hospital, Salt Lake City | 28 |
| United States | UT Southwestern Medical Center, Texas | 6 |
| United States | St. Louis Children's Hospital, St. Louis | 16 |
| Total | | 1601 |