SafeBoosC-III newsletter March 2021

Dear investigators

Welcome to the March 2021 issue of the SafeBoosC-III newsletter.

Blinding and non-byline authorship for co-investigators in the SafeBoosC-III follow-up study
The SafeBoosC-III two year follow up will rely on routine clinical data as well as parental questionnaires. Blinding of the clinical examinations is not possible, but it is unlikely that these clinicians will be biased regarding the SafeBoosC allocation group. However, it is possible to blind the data entries. On the Steering Committee meeting the 22nd of March, it was decided that the PI should delegate the review of the clinical files of the child to a competent colleague, who then is to perform the data entries in OpenClinica blinded.

This will require that each NICU should develop a blinding procedure to be approved centrally. The PI will be given a regular co-authorship, and the blinded two-year outcome assessor will be given a non-byline authorship. This will, for the blinded assessor, mean that their name will not appear in the byline, but will be stated in acknowledgements and would furthermore appear in a PubMed search. We believe this pragmatic approach will strengthen the quality of the follow-up study.

Extra classification of retinopathy of prematurity in OpenClinica
As mentioned in a previous e-mail, after realizing that early ROP treatment may prevent the disease to develop into stage 3, it has been decided by the steering committee, to add a second coding of retinopathy of prematurity (ROP) in OpenClinica:

ROP-no-treatment = 0 ROP-treatment = 1

The decision was taken at the latest steering committee meeting on 22nd of March. This change should not mean much extra work for future infants but requires that all investigators add the data into OpenClinica, for the babies where follow-up data forms have already been completed.

Once again, we apologize for this extra work. Gorm relied on the classical staging (pre-threshold CRYOROP), when planning SafeBoosC-II and III. However, more and more ophthalmologists use the ETROP criteria. Elzbieta in Krakow brought this to our attention, and several of you have supported that it is a real problem.

Completion of data entries for the extra classification of ROP, will be monitored during the monthly central monitoring and investigators with incomplete data entries will be notified.

First interim analysis completed
The Data Monitoring and Safety Committee, chaired by Andrew Whitelaw, Emeritus Professor of Neonatal Medicine at University of Bristol, and including Professor James Boardmann, Edinbourgh and professor, statistician Theis Lange, Copenhagen University, have conducted the first interim analyse. The committee unanimously conclude that the trial should continue and that there is no reason to conduct a second interim analysis.

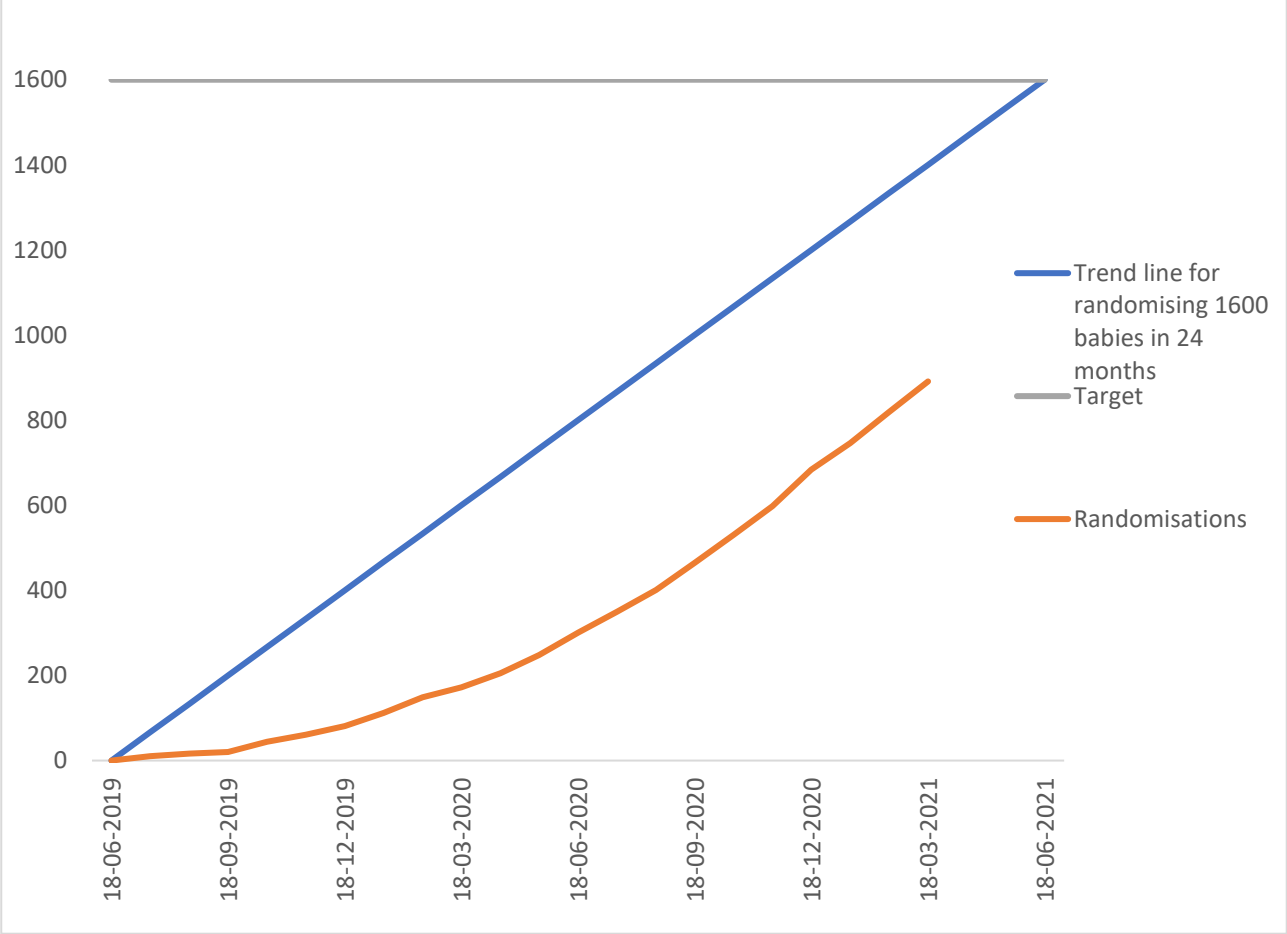
The official letter from the Data Monitoring and Safety Committee is available on the webpage:

https://www.rigshospitalet.dk/english/departments/juliane-marie-centre/department-of-neonatology/research/SafeboosC-III/Documents/dmsc-letter.pdf

Status on randomisations and trial preparations

As of the 18th of March, a total of 891 babies have been randomised across 67 centres (fig. 1). Thus, the randomisation rate has increased (2.55 per day) , from 2.35 in February, and five new centres are randomising. If we continue with the present randomisation rate, we will complete recruitment before the end of 2021.

Figure 1. Randomisations in the SafeBoosC-III trial



In **table 1** below, you will find an overview of the randomisations in each of the 67 centres up until 18th of March 2021. You will also find an overview of the average number of randomisations per month for each centre during the time period, where the hospital has been open for randomisation.

Table 1. Open centres, randomisations and average randomisations per month per centre up until 18th of March 2021.

Country	Centre	Randomised since	Randomisations	Randomisations per month
Austria	University Hospital Graz	Jun 2020	12	1.3
Belgium	UZ Leuven	Jun 2020	24	2.7
Belgium	Liege Rocourt	Jul 2020	10	1.3
Belgium	Grand Hospital de Charleroi	Jul 2020	5	0.6
Belgium	AZ St. Jan University Hospital Brugge	Sep 2020	7	1.2
Belgium	CHU Tivoli	Sep 2020	9	1.5
Belgium	Liege Citadelle Hospital	Nov 2020	0	0
Czech Republic	The Institute for the Care of Mother and Child	Sep 2019	46	2.6
Czech Republic	Motol University Hospital	February 2021	1	1
China	Children's Hospital of Zhejiang, Hangzhou	Jan 2020	2	0.1
China	Children's Hospital of Fudan University, Shanghai	Jan 2020	35	2.5
China	Hainan Women and Children's Medical Center	Mar 2020	0	0
China	Guangzhou Women and Children's Medical Center	Mar 2020	2	0.2
China	Longgang District Central Hospital of Shenzen	May 2020	7	0.7
China	The People's Hospital of Dehong	May 2020	3	0.3
China	Guangxi Maternal and Child Healthcare Hospital, Nanning	May 2020	5	0.5
China	Xiamen Children's Hospital	May 2020	2	0.2
Denmark	Rigshospitalet	Jun 2019	78	3.7
Denmark	Odense University Hospital	Dec 2019	9	0.6
Denmark	Aalborg University Hospital	Mar 2020	8	0.7
Denmark	Aarhus University Hospital	May 2020	10	1
Germany	Freiburg University Hospital	June 2020	6	0.7
Greece	Ippokrateion General Hospital of Thessaloniki	Oct 2019	25	1.5
Greece	University of Patras General Hospital	Jan 2020	8	0.6
Greece	Alexandra Univ. Hospital	Mar 2020	13	1.1
Greece	University Hospital of Heraklion	Mar 2020	8	0.7

Country	Centre	Randomised since	Randomisations	Randomisations per month
India	St Johns Medical College Hospital, Bangalore	Jun 2020	3	0.3
Ireland	University Hospital Cork	February 2021	3	3
Italy	Fondazione IRCCS Cà Granda Ospedale, Milano	Nov 2019	31	1.9
Italy	Presidio Ospedaliero S. Anna, Turin	Aug 2020	3	0.4
Italy	Ospedale Fillipo del Ponte, Varese	Oct 2020	4	0.8
Italy	Fondazione Policlinico Univ. A. Gemelli, Roma	Dec 2020	4	1.3
Poland	Medical Center UJASTEK, Krakow	Jan 2020	24	1.7
Poland	Szpital Uniwersytecki, Kraków	Oct 2020	4	0.8
Poland	Warsaw University of Medical Sciences	Oct 2020	4	0.8
Poland	Poznan University of Medical Sciences	Mar 2020	23	1.9
Poland	Specialist Hospital No. 2 in Bytow	Feb 2020	3	0.2
Poland	Wroclaw Medical University	Apr 2020	0	0
Poland	Jan Biziel University Hospital	Sep 2020	0	0
Spain	H. Univ. Juan XXIII de Tarragona Hospital	Feb 2020	11	0.8
Spain	La Paz University Hospital	Jul 2019	60	3.0
Spain	Hospital Clinic de Barcelona	Jul 2019	37	1.9
Spain	University Hospital 12 de Octubre	Jul 2019	38	1.9
Spain	Hospital de Sant Joan de Deu	Oct 2019	24	1.4
Spain	Hospital Clinico San Carlos	Sep 2019	25	1.4
Spain	Hospital Universitarie Puerta del Mar	Oct 2019	17	1
Spain	H. Universitario Marqués de Valdecilla	Dec 2019	14	0.9
Spain	H. U. Virgen de las Nieves, Granada	Jan 2020	6	0.4
Spain	C. U. Universitario de Santiago	Jan 2020	0	0
Spain	Hospital Miguel Servet	Apr 2020	0	0
Spain	Hospital de Cruces	Jan 2021	1	0.5
Switzerland	Zürich University Hospital	Dec 2019	33	2.2
Switzerland	Luzerner Kantonsspital	Jan 2020	31	2.2
Switzerland	Geneva University Hospital	May 2020	8	0.8
Switzerland	Lausanne University Hospital	Sep 2020	13	2.2
Turkey	Gazi University Hospital	Jan 2020	10	0.7

Country	Centre	Randomised since	Randomisations	Randomisations per month
Turkey	Marmara University Hospital	Jan 2020	20	1.4
Turkey	Uludag University Hospital	Jan 2020	19	1.4
Turkey	Kanuni Sultan University Hospital	Jan 2020	11	n/a
Turkey	Bilkent Integrated Health Care Campus	Jan 2020	30	2.1
Turkey	Basaksehir City Hospital	Jan 2021	1	0.5
United Kingdom	Royal Hospital for Children, Glasgow	Feb 2021	3	1
United Kingdom	NHS Lanarkshire Hospital, Wishaw	March 2021	1	1
United States	University of Utah, Division of Neonatology	Jun 2020	12	1.3
United states	Loma Linda University Hospital	Sep 2020	21	3.5
United States	UT Southwestern Medical Center, Dallas	Oct 2020	3	0.6
Total			891	

Minutes from Steering committee meeting
The twelfth steering committee meeting was held on 22nd of March through the online platform Zoom. The minutes from the meeting can be found here:

https://www.rigshospitalet.dk/english/departments/juliane-marie-centre/department-of-neonatology/research/SafeboosC-III/Documents/minutes-from-safeoos-c-iii-steering-committee-meeting-march-2021.pdf

Data completion monitoring report
In the link below you will find the central monitoring report on data completion from March 2021.

https://www.rigshospitalet.dk/english/departments/juliane-marie-centre/department-of-neonatology/research/SafeboosC-III/Documents/for-professionals/data-completion-report-18-mar-2021.pdf

For the end of monitoring and follow-up form, completion of data entries is still good with 97% completion for both forms. Completion of the blinded follow-up form has increased from 90% last month to 91% this month. However, completion of the SAR form has decreased from 93% to 92% this month. Thus, completion rates are still fairly good, despite the number of recruited babies increases. However, as we aim for less than five percent missing data, there is still room for improvement.

Once again, we would like to state that timely reporting is an important part of the quality of the trial and thus we hope you will prioritize these data entries despite your busy daily schedule.

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

Best wishes
Gorm and Mathias