

SafeBoosC-III newsletter October 2020

Dear investigators

Welcome to the October 2020 issue of the SafeBoosC-III newsletter.

First interim analysis in February 2021

As we have almost randomised one third (533) of the 1600 babies, the Data Monitoring and Safety Committee have started to plan the first interim analysis, which will take place when all 533 babies have reached 36 weeks of postmenstrual age, plus an extra four weeks for data entry. We expect that the analysis will take place mid-February 2021.

It is very important that all data is entered on the 533 babies before the analysis takes place, thus we urge all of you to complete data entries in time.

Extremely preterm infant admissions within the SafeBoosC-III consortium during the COVID-19 lockdown

The manuscript of the observational study, evaluating if the number of admitted extremely preterm infants has changed in the NICUs of the SafeBoosC-III consortium during the global lockdown period, when compared to the corresponding time period in 2019, has been uploaded and published at MedRxiv. The study found no significant difference in the number of extremely preterm infant admissions between the two time periods. Furthermore, no significant difference was seen within geographic regions. The manuscript can be found in the link below:

www.medrxiv.org/content/10.1101/2020.10.02.20204578v1

It was initially submitted to Arch Dis Child, Fetal Neonatal Ed. since they had previously published a paper on this topic, presenting a decrease in the birth rate of extremely preterm infants in Denmark, during the first wave of COVID-19. However, the editor turned the manuscript down, with the following argument:

"We receive many more papers than we have room to publish and can only accept a minority. We felt that your study was well-presented but that the results would not have a strong enough influence on our readers for it to win priority for acceptance ahead of other papers under consideration at this time. It will be important for population based studies to assess the impact of the pandemic on preterm birth and outcomes. It is complex looking at this in populations from a range of countries, with different healthcare organisation, different social provision and different degrees of lockdown. Important differences in some systems may not be present in others. Combining data may not be appropriate. Consequently it is difficult to generalise conclusions from this study."

Personally, we disagree with his statement, as it is difficult to reach a sufficient sample size in this population, without combining data from multiple hospitals. SafeBoosC-III is a good example on this, as we will need 1600 babies in order to obtain a sufficient sample size. Thus, it is necessary to combine data from many hospitals from different geographical regions.

The manuscript will now be submitted to PlosOne.

Online overview of local funding

A list of local funders is now available online:

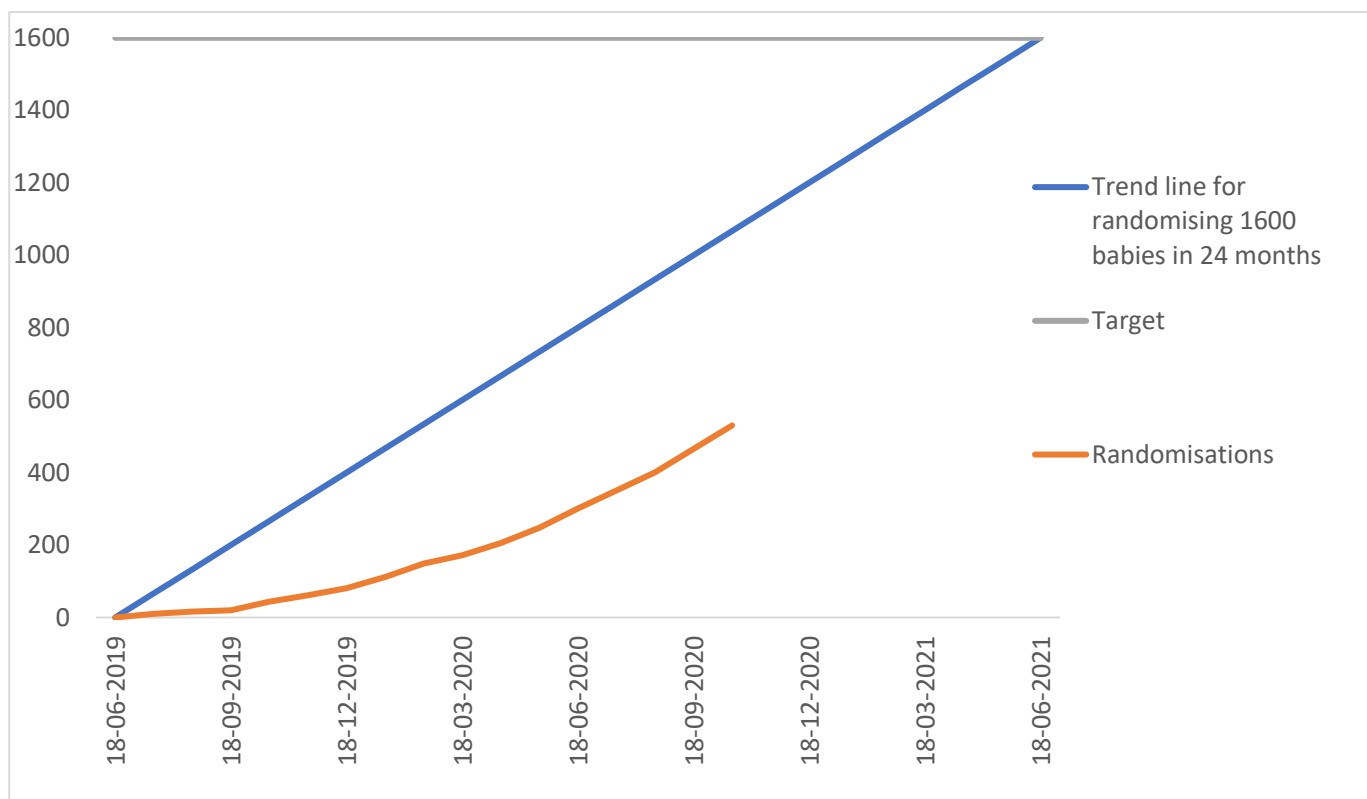
<https://www.rigshospitalet.dk/english/departments/juliane-marie-centre/department-of-neonatology/research/SafeboosC-III/Documents/overview-of-local-funding-within-nicus-participating-in-the-safeboosc-iii-trial.pdf>

We will continuously update the list, when we obtain new information from those of you, who have not provided us with information on local funding yet.

Status on randomisations and trial preparations

As of the 18th of October, a total of 530 babies have been randomised, which is, once again, an increase compared to last month (2.17 randomised babies per day compared to 2.02 randomised babies per day in September) (**figure 1**). At the same time, the number of hospitals open for randomisation has increased from 54 to 58.

Figure 1. Randomisations in the SaeBoosC-III trial



If we continue with the present randomisation rate, we will complete recruitment by February 2022. However, seven of the 58 hospitals have been randomising for less than five weeks, and we also expect that at least ten additional hospitals will start randomising before the end of 2020. Thus, it is probably realistic to complete recruitment before the end of 2021.

In **table 1** below, you will find an overview of the randomisations in each of the 58 open hospitals up until 18th of October 2020. Overall, there is a trend that the recruitment in the hospital of the national coordinator is higher than in other hospitals in the same country. This may be due to an earlier start, to higher admission rates, or may indicate room for improvement. We suggest that national coordinators and principal investigators at each hospital consider the possibilities.

Table 1. Open hospitals and randomisations up until 18th of September 2020.

Country	Centre	Randomised since	Randomisations
Austria	University Hospital Graz	Jun 2020	2
Belgium	UZ Leuven	Jun 2020	10
Belgium	Liege Rocourt	Jul 2020	1
Belgium	Grand Hospital de Charleroi	Jul 2020	4
Belgium	AZ St. Jan University Hospital Brugge	Sep 2020	0
Belgium	CHU Tivoli	Sep 2020	3
Czech Republic	The Institute for the Care of Mother and Child	Sep 2019	34
China	Children's Hospital of Zhejiang, Hangzhou	Jan 2020	0
China	Children's Hospital of Fudan University, Shanghai	Jan 2020	22
China	Hainan Women and Children's Medical Center	Mar 2020	0
China	Guangzhou Women and Children's Medical Center	Mar 2020	1
China	Longgang District Central Hospital of Shenzhen	May 2020	3
China	The People's Hospital of Dehong	May 2020	1
China	Guangxi Maternal and Child Healthcare Hospital, Nanning	May 2020	1
China	Xiamen Children's Hospital	May 2020	1
Denmark	Rigshospitalet	Jun 2019	63
Denmark	Odense University Hospital	Dec 2019	3
Denmark	Aalborg University Hospital	Mar 2020	3
Denmark	Aarhus University Hospital	May 2020	4
Germany	Freiburg University Hospital	June 2020	3
Greece	Ippokrateion General Hospital of Thessaloniki	Oct 2019	18
Greece	University of Patras General Hospital	Jan 2020	7
Greece	Alexandra Univ. Hospital	Mar 2020	9
Greece	University Hospital of Heraklion	Mar 2020	4

Country	Centre	Randomised since	Randomisations
India	St Johns Medical College Hospital, Bangalore	Jun 2020	1
Italy	Fondazione IRCCS Cà Granda Ospedale Maggiore Policlinico, Milano	Nov 2019	16
Italy	Presidio Ospedaliero S. Anna, Turin	Aug 2020	1
Italy	Ospedale Filippo del Ponte, Varese	Oct 2020	0
Poland	Medical Center UJASTEK, Krakow	Jan 2020	13
Poland	Szpital Uniwersytecki, Kraków	Oct 2020	0
Poland	Warsaw University of Medical Sciences	Oct 2020	0
Poland	Poznan University of Medical Sciences	Mar 2020	14
Poland	Specialist Hospital No. 2 in Bytow	Feb 2020	3
Poland	Wroclaw Medical University	Apr 2020	0
Poland	Jan Biziel University Hospital	Sep 2020	0
Spain	H. Univ. Juan XXIII de Tarragona Hospital	Feb 2020	9
Spain	La Paz University Hospital	Jul 2019	41
Spain	Hospital Clinic de Barcelona	Jul 2019	31
Spain	University Hospital 12 de Octubre	Jul 2019	32
Spain	Hospital de Sant Joan de Deu	Oct 2019	19
Spain	Hospital Clinico San Carlos	Sep 2019	15
Spain	Hospital Universitarie Puerta del Mar	Oct 2019	12
Spain	H. Universitario Marqués de Valdecilla	Dec 2019	9
Spain	H. U. Virgen de las Nieves, Granada	Jan 2020	5
Spain	C. U. Universitario de Santiago	Jan 2020	0
Spain	Hospital Miguel Servet	Apr 2020	0
Switzerland	Zürich University Hospital	Dec 2019	19
Switzerland	Luzerner Kantonsspital	Jan 2020	17
Switzerland	Geneva University Hospital	May 2020	5
Switzerland	Lausanne University Hospital	Sep 2020	0
Turkey	Gazi University Hospital	Jan 2020	5
Turkey	Marmara University Hospital	Jan 2020	13
Turkey	Uludag University Hospital	Jan 2020	13
Turkey	Kanuni Sultan University Hospital	Jan 2020	11
Turkey	Bilkent Integrated Health Care Campus	Jan 2020	24
United States	University of Utah, Division of Neonatology	Jun 2020	2
United states	Loma Linda University Hospital	Sep 2020	4
United States	UT Southwestern Medical Center, Dallas	Oct 2020	0
Total			530

Data completion monitoring report

In the link below you will find the central monitoring report regarding data completion from October 2020.

<https://www.rigshospitalet.dk/english/departments/juliane-marie-centre/department-of-neonatology/research/SafeboosC-III/Documents/for-professionals/data-completion-report-19-oct-2020.pdf>

For the end of monitoring and follow-up form, completion of data entries is still good with 95% and 99% completion respectively. Completion of the blinded follow-up form has slightly improved from 84% last month to 87% this month. However, there is still room for improvement, as we aim for less than five percent missing data.

The completion of the SAR form as increased well since last month, with 89% completed SAR forms compared to 56% last month. As this is only the second month where we monitor completion of SAR forms, we are quite sure that the completion percentage will be even higher in November.

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.

Thank you for your time,

Best wishes

Gorm and Mathias