SafeBoosC-III newsletter July 2021

Dear investigators

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

Two new publications from the SafeBoosC-III consortium

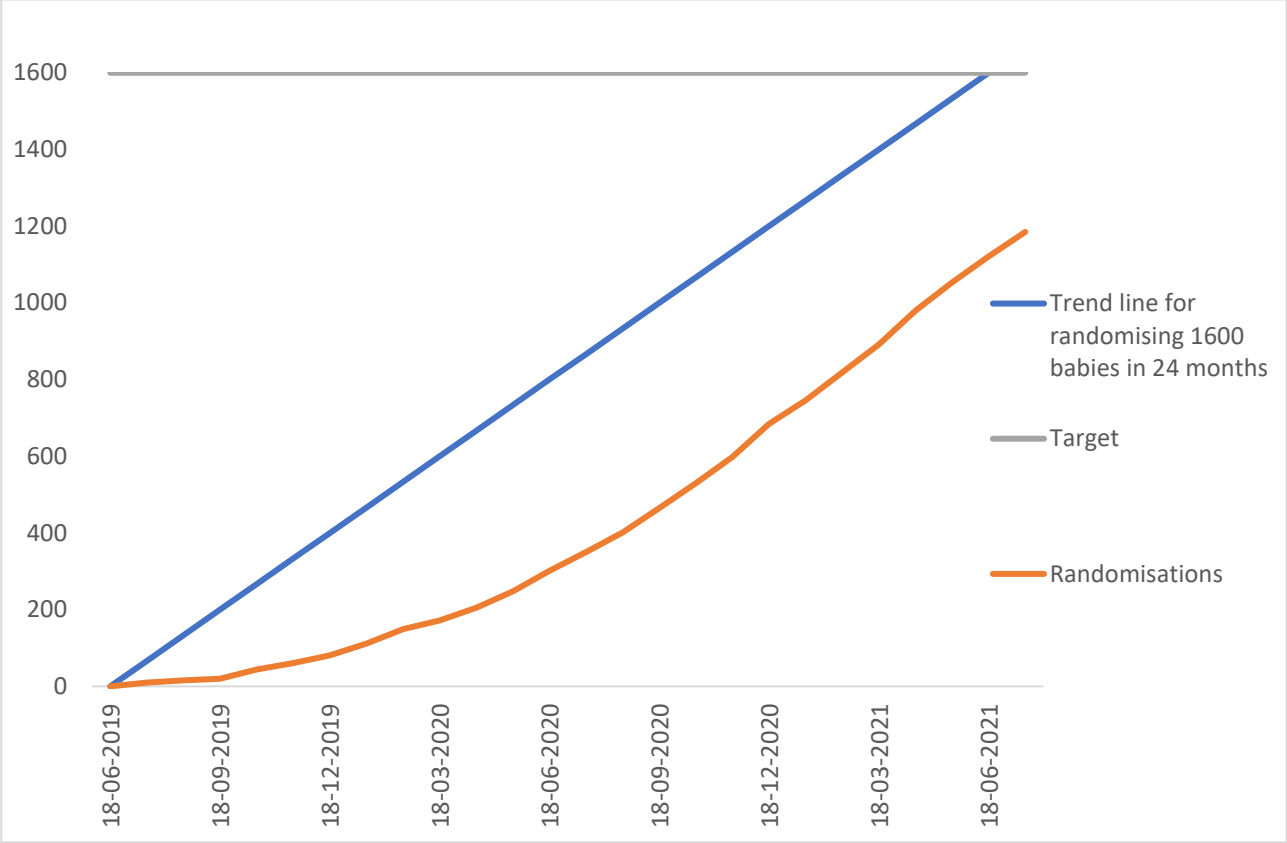
On the 12th of July, the manuscript "Extremely preterm infant admissions within the SafeBoosC-III consortium during the COVID-19 lockdown" was published in Frontiers in Pediatrics (https://www.frontiersin.org/articles/10.3389/fped.2021.647880/full). The road to publishing this manuscript has been long. In October 2020, it was submitted to Arch dis Child, since we thought it would be interesting to their readers, as Arch Dis Child published one of the first papers on this topic (https://fn.bmj.com/content/106/1/93). The editor unfortunately declined our manuscript. Following this, the manuscript was submitted to both JAMA Pediatrics and PLOS ONE who also declined it. As for Arch Dis Child and JAMA, the editors did not believe that the manuscript would be of interest to their readers, while PLOS ONE rejected it based on peer-reviewer comments. We believe that our 'negative' findings were the main reason for the declines. Editors of biomedical journals are dependent on their readers, and readers like breaking news, i.e. 'positive findings'. Based on this experience, Gorm, Lina, Marie and Mathias are in the process of writing a commentary on publication bias of negative results.

On the 8th of July, the manuscript "Central data monitoring in the multicentre randomised SafeBoosC-III trial – a pragmatic approach" was accepted for publication in BMC Medical Research Methodology. It has not been published online yet. Markus Harboe Olsen, a medical doctor from Copenhagen Trial Unit who is part of the SafeBoosC-III central data monitoring group, has taken the lead on this manuscript.

Status on randomisations and trial preparations

As of the 18th of July, a total of 1185 babies have been randomised across 71 centres (fig. 1). This corresponds to 2.1 randomised babies per day, which is a decrease, when compared to the last three months. In April, the randomisation rate reached an all-time high with 2.9 randomised babies per day. In May, it dropped to 2.4 and in June it was 2.2. The previous aim was to complete recruitment before the end of 2021, but if the randomisation rate does not increase again, this will be difficult. Let us hope that we can improve recruitment and thus, complete the trial 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 71 centres up until 18th of July 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 July 2021.

Country	Centre	Randomised since	Randomisations	Average randomisations per month
Austria	University Hospital Graz	Jun 2020	14	1.1
Belgium	UZ Leuven	Jun 2020	26	2.0
Belgium	Liege Rocourt	Jul 2020	19	1.6
Belgium	Grand Hospital de Charleroi	Jul 2020	7	0.6
Belgium	AZ St. Jan University Hospital Brugge	Sep 2020	10	1.0
Belgium	CHU Tivoli	Sep 2020	13	1.3
Belgium	Liege Citadelle Hospital	Nov 2020	0	0

Country	Centre	Randomised since	Randomisations	Average randomisations per month
Czech Republic	The Institute for the Care of Mother and Child	Sep 2019	54	2.5
Czech Republic	Motol University Hospital	February 2021	4	0.8
China	Children's Hospital of Zhejiang, Hangzhou	Jan 2020	4	0.2
China	Children's Hospital of Fudan University, Shanghai	Jan 2020	35	1.9
China	Hainan Women and Children's Medical Center	Mar 2020	2	0.1
China	Guangzhou Women and Children's Medical Center	Mar 2020	2	0.1
China	Longgang District Central Hospital of Shenzen	May 2020	10	0.7
China	The People's Hospital of Dehong	May 2020	3	0.2
China	Guangxi Maternal and Child Healthcare Hospital, Nanning	May 2020	7	0.5
China	Xiamen Children's Hospital	May 2020	4	0.3
Denmark	Rigshospitalet	Jun 2019	85	3.4
Denmark	Odense University Hospital	Dec 2019	9	0.5
Denmark	Aalborg University Hospital	Mar 2020	14	0.9
Denmark	Aarhus University Hospital	May 2020	16	1.1
Germany	Freiburg University Hospital	June 2020	10	0.8
Greece	Ippokrateion General Hospital of Thessaloniki	Oct 2019	31	1.6
Greece	University of Patras General Hospital	Jan 2020	10	0.5
Greece	Alexandra Univ. Hospital	Mar 2020	13	0.8
Greece	University Hospital of Heraklion	Mar 2020	8	0.5
India	St Johns Medical College Hospital, Bangalore	Jun 2020	4	0.3
Ireland	University Hospital Cork	February 2021	16	3.2
Ireland	Rotunda Hospital Dublin	May 2021	3	1.5
Ireland	NMH Holles St	May 2021	4	2
Ireland	Coombe Univ. Hospital	May 2021	4	2
Italy	Fondazione IRCCS Cà Granda Ospedale, Milano	Nov 2019	38	1.9
Italy	Presidio Ospedaliero S. Anna, Turin	Aug 2020	5	0.5

Country	Centre	Randomised since	Randomisations	Average randomisations per month
Italy	Ospedale Fillipo del Ponte, Varese	Oct 2020	4	0.4
Italy	Fondazione Policlinico Univ. A. Gemelli, Roma	Dec 2020	8	1.1
Norway	Oslo University Hospital	March 2021	16	4
Poland	Medical Center UJASTEK, Krakow	Jan 2020	32	1.8
Poland	Szpital Uniwersytecki, Kraków	Oct 2020	14	1.6
Poland	Warsaw University of Medical Sciences	Oct 2020	9	1.0
Poland	Poznan University of Medical Sciences	Mar 2020	28	1.8
Poland	Specialist Hospital No. 2 in Bytow	Feb 2020	6	0.4
Poland	Wroclaw Medical University	Apr 2020	0	0
Poland	Jan Biziel University Hospital	Sep 2020	0	0
Poland	Centre of Medical Postgraduate Education, Warsaw	May 2021	4	2
Spain	H. Univ. Juan XXIII de Tarragona Hospital	Feb 2020	15	0.9
Spain	La Paz University Hospital	Jul 2019	68	2.8
Spain	Hospital Clinic de Barcelona	Jul 2019	47	2.0
Spain	University Hospital 12 de Octubre	Jul 2019	57	2.4
Spain	Hospital de Sant Joan de Deu	Oct 2019	26	1.2
Spain	Hospital Clinico San Carlos	Sep 2019	29	1.3
Spain	Hospital Universitarie Puerta del Mar	Oct 2019	18	0.9
Spain	H. Universitario Marqués de Valdecilla	Dec 2019	17	0.9
Spain	H. U. Virgen de las Nieves, Granada	Jan 2020	11	0.6
Spain	C. U. Universitario de Santiago	Jan 2020	0	0
Spain	Hospital Miguel Servet	Apr 2020	0	0
Spain	Hospital de Cruces	Jan 2021	2	0.3
Switzerland	Zürich University Hospital	Dec 2019	37	2.3 (withdrew in May 2021)
Switzerland	Luzerner Kantonsspital	Jan 2020	34	1.9
Switzerland	Geneva University Hospital	May 2020	9	0.6
Switzerland	Lausanne University Hospital	Sep 2020	16	1.6
Turkey	Gazi University Hospital	Jan 2020	13	0.7
Turkey	Marmara University Hospital	Jan 2020	29	1.6

Country	Centre	Randomised since	Randomisations	Average randomisations per month
Turkey	Uludag University Hospital	Jan 2020	31	1.7
Turkey	Kanuni Sultan University Hospital	Jan 2020	11	1 (withdrew in December 2020)
Turkey	Bilkent Integrated Health Care Campus	Jan 2020	36	2.0
Turkey	Basaksehir City Hospital	Jan 2021	8	1.3
United Kingdom	Royal Hospital for Children, Glasgow	Feb 2021	10	2.0
United Kingdom	NHS Lanarkshire Hospital, Wishaw	March 2021	4	1.0
United States	University of Utah, Division of Neonatology	Jun 2020	17	1.3
United States	Loma Linda University Hospital	Sep 2020	26	2.6
United States	UT Southwestern Medical Center, Dallas	Oct 2020	6	0.7
United States	Washington Univ. Hospital	June 2021	3	3
Total			1185	

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

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

For the end of monitoring and serious adverse reactions (SAR) forms, completion of data entries has decreased from last month, to 97% (-1%) and 91% (-4%) respectively. We believe that part of this can be explained by the technical errors in OpenClinica, which we experienced earlier in July. The technical errors occurred in the process implementing the eCRF for the two-year follow-up study. To fix this, the end of monitoring and SAR forms were blocked for data entries for a week.

As for the 36 weeks follow-up form, data completion is still high (99%). Completion of the blinded follow-up form has also increased to 90% (+1%).

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

Update on funding for the SafeBooSC-III follow-up study and the SafeBoosC-IIIv trial
In April, we submitted a grant application to Innovation Fund Denmark, to cover the central study costs for the SafeBoosC-III follow-up study, and the SafeBoosC-IIIv trial. The total amount that we applied for, was 1.3 million euro. In June, we unfortunately received a rejection. Even though, the Innovation Fund described the two studies as “very intriguing and well described in comparison with the state of art” and considered the plan for implementation of the results to be “addressed in a satisfactory way”, the expected value creation

was not considered sufficiently compelling for an investment, given the strong competition (many applications to the call).

As for now, we intend to submit a grant application to the Novo Nordisk foundation (Investigator Initiated Trials call) before the deadline, which is the 1st of September.

The SafeBoosC project at jENS 2021

During the jENS 2021 online conference, which takes place between 14th and 18th of September, the SafeBoosC project will be widely represented. Mathias has been invited as a speaker and will focus on the SafeBoosC-III trial during his talk on the 16th of September at 15:30 CET (Workshop no. 4, NIRS-circulation-PDA). Marie submitted an abstract on the SafeBoosC-III follow-up study, which has been selected as a poster, and an abstract on the SafeBoosC-III COVID study (https://www.frontiersin.org/articles/10.3389/fped.2021.647880/full), which has been selected for oral presentation on the 17th of September at 10:00 CET (parallel session 25 – UENPS 2). Maria submitted an abstract on the SafeBoosC-IIIv trial, which has also been selected as a poster.

Best wishes
Gorm, Marie, Maria and Mathias