

SafeBoosC-III newsletter June 2021

Dear investigators

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

NIRS monitoring before randomisation –equipoise?

During the present round of central data monitoring, we have encountered a number of cases, where a baby has been registered with start of NIRS monitoring before randomisation. In some cases, it was due to a data entry error. In other cases, NIRS monitoring was started before randomisation, since the neonatologist judged that it would benefit the baby. It is not a protocol violation, since the monitoring was conducted outside of the intervention period (which is from randomisation and until 72 hours of age). Such initial monitoring, however, should not delay randomisation, since the protocol states that monitoring should be initiated *“as soon as possible after birth, and always within six hours...:”*.

More importantly, this is a question of equipoise. If you, or any of your colleagues think that NIRS monitoring before randomisation is beneficial, you may not be in equipoise as to the intervention. When planning SafeBoosC-III we were aware that equipoise may be a problem, and some NICUs do not participate because of this.

Most importantly, clinical use of NIRS outside the SafeBoosC-III protocol may contribute to the loss of equipoise among staff (and parents) so it is important that you discuss this among your colleagues and that we maintain full transparency and discuss this within the SafeBoosC-consortium.

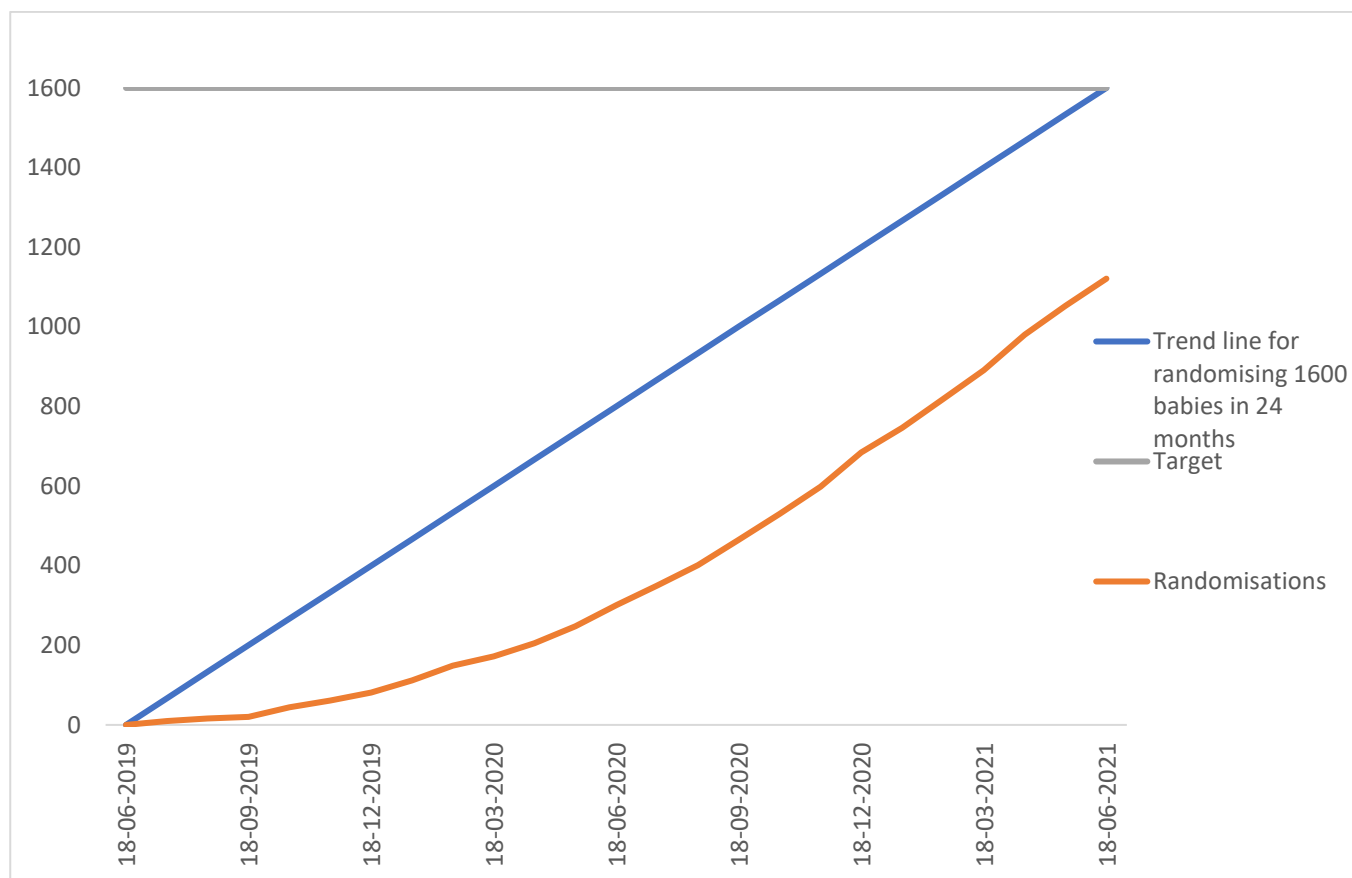
Therefore, please do not hesitate to reach out to us, if equipoise has started to slip in your centre. We also recommend all of you to read the paper on equipoise by Gorm and Frank Van Bel:

<https://onlinelibrary.wiley.com/doi/epdf/10.1111/apa.13549> (attached in e-mail also).

Status on randomisations and trial preparations

As of the 18th of June, a total of 1121 babies have been randomised across 71 centres (fig. 1). This corresponds to 2.2 randomised babies per day, which is a decrease when compared to April (2.9 randomised babies per day) and May (2.4 randomised babies per day). If we continue with an average of 2.2 babies per day, we will not complete recruitment until the end of January. Therefore, 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 June 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 June 2021.

Country	Centre	Randomised since	Randomisations	Average randomisations per month
Austria	University Hospital Graz	Jun 2020	14	1.2
Belgium	UZ Leuven	Jun 2020	25	2.1
Belgium	Liege Rocourt	Jul 2020	19	1.7
Belgium	Grand Hospital de Charleroi	Jul 2020	6	0.5
Belgium	AZ St. Jan University Hospital Brugge	Sep 2020	10	1.1
Belgium	CHU Tivoli	Sep 2020	13	1.4
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	53	2.5
Czech Republic	Motol University Hospital	February 2021	4	1
China	Children's Hospital of Zhejiang, Hangzhou	Jan 2020	4	0.2
China	Children's Hospital of Fudan University, Shanghai	Jan 2020	35	2.1
China	Hainan Women and Children's Medical Center	Mar 2020	1	0.05
China	Guangzhou Women and Children's Medical Center	Mar 2020	2	0.1
China	Longgang District Central Hospital of Shenzhen	May 2020	10	0.8
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	84	3.5
Denmark	Odense University Hospital	Dec 2019	9	0.5
Denmark	Aalborg University Hospital	Mar 2020	14	0.9
Denmark	Aarhus University Hospital	May 2020	14	1.1
Germany	Freiburg University Hospital	June 2020	10	0.8
Greece	Ippokrateion General Hospital of Thessaloniki	Oct 2019	28	1.5
Greece	University of Patras General Hospital	Jan 2020	10	0.6
Greece	Alexandra Univ. Hospital	Mar 2020	13	0.9
Greece	University Hospital of Heraklion	Mar 2020	8	0.5
India	St Johns Medical College Hospital, Bangalore	Jun 2020	3	0.3
Ireland	University Hospital Cork	February 2021	11	2.8
Ireland	Rotunda Hospital Dublin	May 2021	2	2
Ireland	NMH Holles St	May 2021	3	3
Ireland	Coombe Univ. Hospital	May 2021	1	1
Italy	Fondazione IRCCS Cà Granda Ospedale, Milano	Nov 2019	34	1.8
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	0.5
Italy	Fondazione Policlinico Univ. A. Gemelli, Roma	Dec 2020	7	1.2
Norway	Oslo University Hospital	March 2021	8	2.7
Poland	Medical Center UJASTEK, Krakow	Jan 2020	32	1.9
Poland	Szpital Uniwersytecki, Kraków	Oct 2020	11	1.4
Poland	Warsaw University of Medical Sciences	Oct 2020	9	1.1
Poland	Poznan University of Medical Sciences	Mar 2020	27	1.8
Poland	Specialist Hospital No. 2 in Bytow	Feb 2020	5	0.3
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	2	2
Spain	H. Univ. Juan XXIII de Tarragona Hospital	Feb 2020	14	0.9
Spain	La Paz University Hospital	Jul 2019	66	2.9
Spain	Hospital Clinic de Barcelona	Jul 2019	47	2.0
Spain	University Hospital 12 de Octubre	Jul 2019	53	2.3
Spain	Hospital de Sant Joan de Deu	Oct 2019	26	1.3
Spain	Hospital Clinico San Carlos	Sep 2019	29	1.4
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	0.4
Switzerland	Zürich University Hospital	Dec 2019	37	2.3 (withdrew in May 2021)
Switzerland	Luzerner Kantonsspital	Jan 2020	34	2
Switzerland	Geneva University Hospital	May 2020	8	0.6
Switzerland	Lausanne University Hospital	Sep 2020	16	1.8
Turkey	Gazi University Hospital	Jan 2020	12	0.7
Turkey	Marmara University Hospital	Jan 2020	28	1.6

Country	Centre	Randomised since	Randomisations	Average randomisations per month
Turkey	Uludag University Hospital	Jan 2020	28	1.6
Turkey	Kanuni Sultan University Hospital	Jan 2020	11	1 (withdrew in December 2020)
Turkey	Bilkent Integrated Health Care Campus	Jan 2020	35	2.1
Turkey	Basaksehir City Hospital	Jan 2021	7	1.4
United Kingdom	Royal Hospital for Children, Glasgow	Feb 2021	8	2.0
United Kingdom	NHS Lanarkshire Hospital, Wishaw	March 2021	4	1.3
United States	University of Utah, Division of Neonatology	Jun 2020	15	1.3
United States	Loma Linda University Hospital	Sep 2020	26	2.9
United States	UT Southwestern Medical Center, Dallas	Oct 2020	5	0.6
United States	Washington Univ. Hospital	June 2021	0	0
Total			1121	

Data completion monitoring report

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

<https://www.rigshospitalet.dk/english/departments/juliane-marie-centre/department-of-neonatology/research/SafeboosC-III/Documents/data-completion-report%2022-june-2021.pdf>

For the end of monitoring, serious adverse reactions (SAR), and follow-up form, completion of data entries has increased from last month to 98% (+2%), 95% (+3) and 99% (+1) respectively. This is a very positive result and we hope that all investigators will continue to prioritise timely reporting.

As for the blinded follow-up form, completion of data entries has also increased, from 86% in May to 89% in June. However, there is still room for improvement, since we aim at less than 5% missing data, and since the completion rate for the blinded follow-up form was 92% in April.

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

Best wishes

Gorm, Marie and Mathias