The Data and Safety Monitoring Board (DSMB) for REMED trial

The Data and Safety Monitoring Board (DSMB) is instituted by University Hospital Brno, for advising and providing expertise and recomendations regarding participant safety and data integrity in clinical trial REMED.

1. MEMBERS OF DSMB

The DSMB is composed of experts in the field reflecting the disciplines neccessary for evaluating the data integrity and patient's safety in REMED trial, medical monitor, experts in conducting clinical trials, statisticians, and safety manager. One of the DSMB member´s task is the management and communication among members of the group. of the members of DSMB should be minimally three and up-to seven. If necessary, an ad hoc specialist could be invited on a non-voting basis, if additional expertise is needed . The sponsor representative or other persons that are directly involved in the trial are prohibited to be member of DSMB although they are permitted to attend open DSMB meetings. Vice versa, no member of DSMB is permitted to have direct involvement in the REMED trial conduct. No member of DSMB should have financial, professional, or other interest related to the REMED trial. The actual members of DSMB for REMED Trial are listed in Appendix 1.

2. AGENDA

2.1. The primary **responsibilities** of the DSMB are:

- Review accumulated data for participant safety, study conduct and overal progress
- Make recomendations to the Steering Comittee (SC) of the REMED trial regarding modification and/or termination of the trial.

During the REMED trial, DSMB is responsible for reviewing cumulative study data to assess safety, conduct of the trial, and integrity of the data and scientific validity.

2.2. **Specifically**, DSMB is responsible for:

- Review of data quality and integrity
- Potential amendments and adherence to the study protocol
- Changes in interim Statistical Analysis Plan (SAP) or final SAP
- Reviewing Severe adverse events (SAE)
- Performance of individual centers and opening potentially new centers
- Recruitment of the study
- Evaluating interim and cumulative analysis data regrading efficacy and safety
- Reviewing external factors that might affect participant safety or ethics of the trial, e.g. new scientific data

2.3. **Reports** from the DSMB

After each review of DSMB, specific recomendations regarding trial continuation or termination or potential modification should be included. Specifically, DSMB should recommend:

- Study termination due to serious concerns regarding safety of the subjects, slow enrollemnet or performance
- Study termination if the study objectives are reached upon preplanned study SAP
- Modification of the study protocol based upon review of the data
- Recomendation regarding increasing the planned number of enrolled subjects through the prolonging recruitment time or increasing the study sites and centers

3. COMMUNICATION

Confidentiality must be always kept during the review and recomendations proces of DSMB. Only DSMB members should have access to interim analysis of the study data. DSMB members must also maintain strict confidentiality regarding the overall study results provided.

3.1. Meetings

The specific form and frequency of DSMB meetings may be flexible and depends on several factors. The DSMB chair plus administrator are responsible for communication and planing the meetings and the provision of all appropriate documentation to to the all DSMB members. After each meeting report and recomendations to the SC should be provided.

3.2. Voting

After discussion within DSMB memebers final recommendations should be recorded and identified as the minority or majority recommendation with individual vote tallies.

4. REFERENCES:

1. National Institute of Health, National Institute of Dental and Craniofacial Research, Data and Safety Monitoring Board (DSMB) Guideliness, accesed on 1th of March 2021
   https://www.nidcr.nih.gov/research/human-subjects-research/toolkit-and-education-materials/interventional-studies/data-and-safety-monitoring-board-guidelines#top
2. European Medicines Agency, Committee for Medicinal Products for Human Use, Guideline on Data Monitoring Committee London, 27 July 2005 Doc. Ref. EMEA/CHMP/EWP/5872/03 accesed on 1th of March 2021
   https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-data-monitoring-committees_en.pdf

3. European Medicines Agency, Committee for Medicinal Products for Human Use, Questions and answers on Data Monitoring Committees issues, 17 September 2020 EMA/CHMP/470185/2020, accesed on 1th of March 2021 *https://www.ema.europa.eu/en/documents/scientific-guideline/questions-answers-data-monitoring-committees-issues_en.pdf*
4. National Health and Medical Research Council (2018), Data Safety Monitoring Boards (DSMBs), accesed on 1th of March 2021 *https://www.australianclinicaltrials.gov.au/sites/default/files/content/For%20researchers/Data%20Safety%20Monitoring%20Boards_1.pdf*

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APPENDIX NO.1:

Role	Name	Affiliation
Clinical Expert Chair of DSMB	Petr Štourač, prof., MD, PhD,	Department of Paediatric Anaesthesiology and Intensive Care Medicine, University Hospital Brno and Faculty of Medicine, Masaryk University, Jihlavská 20, Brno, 625 00 Czech Republic
Medical Monitor, Administrator and Vice-chair of DSMB	Milan Kratochvíl, MD, EDIC	Department of Paediatric Anaesthesiology and Intensive Care Medicine, University Hospital Brno and Faculty of Medicine, Masaryk University, Jihlavská 20, Brno, 625 00 Czech Republic
Safety Manager	Kateřina Nerušilová, MD	Department of Pharmacology/CZECRIN, Faculty of Medicine, Masaryk University, Kamenice 5, Brno, 62500 Czech Republic
Statisticians	Ladislav Dušek, prof., RNDr. PhD	Institute of Health Information and Statistics of the Czech Republic, Palackého náměstí 4 128 01 Praha 2
Statisticians	Adam Svobodník, MSc., PhD	Department of Pharmacology Faculty of Medicine, Masaryk University, Kamenice 753/5, 625 00 Brno
Clinical Expert	Mervyn Singer MB BS MD FRCP(Lon) FRCP(Edin) FFICM	University College London, Centre for Intensive Care Medicine, Department of Medicine & Wolfson Institute for Biomedical Research, Gower Street, London, WC1E 6BT, United Kingdom
Clinical Expert	Vladimír Černý, prof. MD, PhD, FCCM	Ministry of Health of the Czech Republic Palackého náměstí 4 128 01 Praha 2

Clinical Expert	Jiří Pařenica, prof., MSc., MD, PhD	Department of Cardiology, University Hospital Brno and Faculty of Medicine, Masaryk University, Jihlavská 20, Brno, 625 00 Czech Republic