Charter for the Data Monitoring and Safety Committee (DMSC) for TRAUMOX2

Version 1.0

Date: 21-12-2021

Comparing Restrictive versus Liberal Oxygen Strategies for Trauma Patients: The TRAUMOX2 Trial

EudraCT number: 2021-000556-19
Danish Research Ethics Committee number: H-21018062
ClinicalTrials.gov number: NCT05146700

Chief investigator and sponsor: Professor Jacob Steinmetz, M.D., Ph.D.

Introduction

This charter will define the responsibilities of the independent DMSC, the members, the purpose of the DMSC and the timing of the meetings. The DMSC is answerable for the safety of trial participants, assessing the safety and efficacy of the interventions during the trial, and for monitoring the overall conduct of the clinical trial. The DMSC is obliged to follow the EU Clinical Trials Directive 2001/20/EC while assessing the study and to keep all patient-level data confidential. The DMSC consists of three clinicians with expertise in critical emergency care research and an independent biostatistician. The DMSC members have been chosen in order to avoid any financial or intellectual conflicts of interest. The members have agreed to this task for the entire duration of the clinical trial. However, should any members leave the DMSC during the trial, the steering committee will appoint the replacement(s). The DMSC is independent from the sponsor and the trial investigators. The DMSC will be notified of all changes to the protocol or changes in trial conduct. The clinicians of the DMSC will be unpaid. The biostatistician will be paid for the hours spent on data analysis prior to the DMSC meetings.

Timing of the meetings

Two interim analysis meetings will be held to review data relating to treatment efficacy, patient safety, and quality of trial conduct (e.g. enrollment progression). The four members of the DMSC will meet either physically or online when 30-day follow-up data (primary outcome) of 355 (approximately 25 % of sample size estimation) and 710 (approximately 50 % of sample size estimation) patients have been obtained. The trial will continue while the DMSC review the data. The DMSC will be specifically notified by e-mail by the sponsor or coordinating investigator when approximately 20 % and 45 % of the patients are included due to scheduling and arranging the first and second meeting. Furthermore, it is optional for the DMSC members to receive the newsletters from the trial. The DMSC will be responsible for scheduling and arranging the meetings. Data will be provided to the DMSC at least 5 days prior to their meetings.

Interim data review

The DMSC will review non-identifiable person data for 30-day mortality at the two predetermined time points. In addition, at the second interim analysis, the DMSC will also consider available data on major lung complications defined as pneumonia and acute respiratory distress syndrome within 30 days after trauma. The DMSC can at any time request extra reviews if necessary. The data will be provided to the biostatistician in Excel. One row will represent one trial participant and each column will be a data variable. The data variables included in the raw data output are:

1: record_id (a number that uniquely identifies the patient)

2: scr_incl_randomisation (the randomisation code: group A or B)

3: outc_prim_spec___1 (occurrence of death within 30 days: 0 = no, 1 = yes)

4: outc_prim_spec___2 (occurrence of pneumonia within 30 days: 0 = no, 1 = yes)

5: outc_prim_spec___3 (occurrence of acute respiratory distress syndrome within 30 days: 0 = no, 1 = yes)

The DMSC statistician will provide aggregate data analysis for variable 3, 4 and 5 in two-by-two tables stratified on variable 2 (renamed randomisation code blinded by an external person). The data provided is only to evaluate on treatment efficacy and patient safety. Thus, no other data variables will be provided.

The DMSC may recommend stopping the trial at each of the two interim analyses if a major difference in 30-day mortality is found. There are no strict stopping criteria, but it is suggested that the recommendation should be based on only a considerable difference, such as a relative risk where the lower limit of the 95 % CI is >2 (regardless of which group is nominator). The same applies to both the first and second interim analysis. There should be no premature ending of the trial for futility before completion of the preplanned inclusion of 1420 patients with a complete 30-day follow-up.

Content of the DMSC reports

After each of the two reviews, the DMSC will produce a short report to the steering committee with recommendations for continuation, modifications, or premature termination of the trial. The DMSC will be advisory to the steering committee. Therefore, the final decision regarding potential modifications or termination will rest with the steering committee.

Members of the DMSC

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Read and agreed by

Bodil Steen Rasmussen

Date: 20-12-2021

Signature: 

Lars Wiuff Andersen

Date: Lars W. Andersen Digitally signed by Lars W. Andersen Date: 2021.12.14 18:20:58 +01'00'

Signature:

Marius Rehn

Date: 13.12.2021

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Brice Ozenne

Date: 19-12-2021

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