The Pre-hospital Anti-fibrinolytics for Traumatic Coagulopathy and Haemorrhage Study
(The PATCH-Trauma Study)

Data Safety Monitoring Committee Charter

1. Purpose

The Data Safety Monitoring Committee (DSMC) is an independent group of advisors that will have confidential access to unblinded complete study data in order to monitor the safety of participants enrolled in the PATCH-Trauma study. The DSMC will subsequently make recommendations to the management committee concerning continuation, termination, or other modification of the trial based on the observed effects of the study drug and adherence to the study protocols.

2. Membership

DSMC members and a chairperson will be appointed by the management committee and will comprise experts in clinical trials, biostatistics and emergency medicine.

3. Conflict of interest

To assure the independence and impartiality of the DSMC, members will have no professional or financial interests dependent on the outcome of the trial. A Conflict of Interest/Confidentiality Disclosure form must be signed by each member of the DSMC. All members should be aware that information included in the interim reports is confidential and must not be disclosed, even partially, either orally or in writing, outside of the committee.

4. Functions

The primary function of the DSMC is to ensure, through advice to the management committee, that the trial is conducted safely and ethically and that it meets its primary objectives. This not only includes the interests of participants already enrolled in the study, but also the interests of future participants and patients outside the study.

a. The DSMC is required to review and approve the study protocol;
b. The DSMC will monitor the benefit and harm of tranexamic acid for participants through a review of the data generated by two interim safety analyses at 25% and 50% of patient enrolment (296 and 592 patients, respectively). Both analyses will examine in-hospital/28-day mortality with a P value for stopping of $P<0.005$. The DSMC will make recommendations about continuing or stopping the trial based on these interim analyses;

c. The DSMC will monitor adherence to trial protocol, in particular the number of patients receiving open-label TXA and the serious adverse event rate among patients receiving more than 2g of TXA as per the protocol;
d. The DSMC may also make other recommendations relating to

- selection, recruitment and management of participants;
- adherence to trial protocols; and
- data management and quality control.

The DSMC statistician will have access to the master randomisation code (provided by the independent pharmaceutical packaging company) to assess the unblinded comparative data for the trial. The code must remain strictly confidential between the DSMC statistician and the pharmaceutical packaging company while the trial is still in progress. The analyses will use the Haybittle-Peto rule applied to mortality data between treatment groups and the conventional 3-standard deviation threshold of a standardised statistic ($|Zk=1| \geq 3$) calculated from a normal approximation to the discrete binomial difference in mortality proportions. Assuming no early stopping, such a single interim Haybittle-Peto analysis will not, in practice, require adjustment (for repeated significance testing) to the conventional statistical significance level ($p<0.05$) to be applied at the final analyses of the completed trial.

5. Meetings

The first meeting of the DSMC will occur prior to patient recruitment for the purpose of discussing and approving the study protocol, reviewing draft case report forms, and establishing the role of individual DSMC members. The DSMC will be scheduled to meet twice throughout the conduct of the study, for the two interim safety analyses, however additional meetings may be arranged when necessary for adequate monitoring. Any member of the committee may also request a meeting to discuss data provided between interim reports.

Closed sessions can only be attended by members of the DSMC and any material presented in these sessions should remain confidential. The committee may wish to invite trial investigators to attend an open session meeting to discuss general issues related to the conduct of the trial, however recommendations of the DSMC should only be discussed and decided on in a closed session of the DSMC.

Minutes of all DSMC meetings (open and closed sessions) must be recorded and may need to be submitted to the relevant regulatory authorities.

6. Interaction with management committee

Following each interim analysis, the Chair of the DSMC will submit a written report to the management committee. The report should document the major points of discussion, any decisions and actions and their reasons, any additional information required at future meetings (where applicable), and the DSMC recommendations concerning continuation, termination, or other modification of the trial based on the DSMC's analyses and deliberations.

7. Interaction with steering committee

In the event the DSMC recommends stopping recruitment, a meeting between the DSMC and steering committee will be held where a final agreement will be sought regarding continuation or termination of the trial.