
**Data and Safety Monitoring Committee (DSMC) Letter**
TESTING DSMB meeting, San Diego November 6th 2015

6th November 2015

Dr Vlado Perkovic
The George Institute for Global Health
Australia

Dear Dr Perkovic,

The TESTING data safety monitoring board met in San Diego on November 6th 2015 to review data on 252 patients randomised into the study. They had the following comments:

- Concern over an imbalance in severe adverse events between the test and control treatment groups and attribution of the majority of the severe adverse events to the test medication, methylprednisolone, has led the DSMB to conclude that the trial should not continue in its current form. We would like to emphasize that our concerns pertain specifically to the emergence of an imbalance of severe adverse events between the randomized groups, and do not at all relate to the conduct of the clinical trial by the study investigators, which has been exemplary.

- If the trial steering committee wishes to continue the trial then we advise:
  - Reducing the dose (overall exposure) of the test medication, by a sufficient amount to reduce the severe adverse event risk.
  - Conducting a physician consultation exercise to explore the degree of risk for severe adverse events and mortality that would be clinically acceptable for the predicted level of benefit.
  - Considering a patient consultation exercise to assess the degree of risk acceptable to patients for the predicted level of benefit.
  - Informing patients in more detail of the risks if they were randomised to the test treatment group.
  - Developing an approach to how the trade off between safety risk and renal benefit can be best presented to the wider community.
  - Reviewing the DSMB membership and considering adding expertise in ethics and risk benefit management.
Stratify subsequent analyses presented to the DSMB according to test dose regimen

- If recruitment to the trial is stopped then we recommend continued follow-up to the planned end of the trial for all randomised patients.
- We recommend further advice to the investigators concerning the risk of severe adverse events including a reduction of test medication/placebo to steroid maintenance low dose levels if an infection occurs.

Other DSMB requests:
- Regardless of whether further recruitment is stopped, to be informed of the plans for management of patients currently in the active treatment phase of the trial and those between screening and randomization.
- More detail on the proportion of severe adverse events that result in chronic morbidity or disability.
- More detail on the time of onset of severe adverse events after initiation of test medication/placebo.
- More statistical analysis detail on the risk versus benefit ratio of the randomized treatment.
- Statistical analysis of the changes in proteinuria between treatment groups.

The DSMB recommends telephone conferences every three months and a face to face meeting in one year. A statistician from the Data Coordinating Center should be present on teleconferences, and should call into face-to-face meetings of the DSMB.

The DSMB appreciate the efforts and success of the trial steering committee in taking the trial to its current status and the high quality conduct of the trial. In their decision they considered the impact of stopping the trial on the wider community and treatment practice.

Yours sincerely,

David Jayne, Chair.

On behalf of the TESTING DSMB
Dr Tom Greene
Dr Michael Walsh
Dr Angela Wang