Terms of reference for Data Monitoring Committee (DMC)

hPOD trial

ACTRN12613000322730

The purpose of this document is to describe the roles and responsibilities of the Data Monitoring Committee (DMC) for the hPOD trial including the timing, frequency and format of meetings, methods of providing information to and from the DMC, statistical issues and relationships with other committees.

Data Monitoring Committee (DMC)

Professor Frank Bloomfield (Chair)

Dr Katie Groom

Mr Greg Gamble (Trial statistician)

Aims

To safeguard the interests of the trial participants, assess the safety and efficacy of the interventions during the trial and monitor the overall conduct of the clinical trial.

Relationships

The DMC will receive reports from the Safety Monitoring Committee (SMC) and reports to the hPOD Trial Steering Committee.

Duties of the DMC

1. To undertake interim analyses of the pre-hPOD (dosage trial), and if required of the hPOD multi-centre trial, including updated figures on recruitment, data quality, and primary outcome and safety data.
2. To make recommendations to the hPOD Trial Steering Committee based on the above review or information from the SMC with regard to early cessation of the trial due to strong evidence of benefit or adverse effect (see discussion of stopping rules below).
3. Examine treatment effects in a blinded manner initially.
4. Advise the hPOD Trial Steering Committee on any additional analyses to be undertaken to assess treatment effects during the trial.

5. Advise the hPOD Trial Steering Committee on operational procedures affecting recruitment, treatment and follow-up.
6. The DMC can be contacted by collaborators and any others associated with the study if considered necessary. Requests for information from Third Parties will be discussed with the hPOD Trial Steering Committee.

Roles and responsibilities

Chair

The Chair will:

i. Co-ordinate and chair meetings
ii. Facilitate and summarise discussions
iii. Keep securely the minutes of the meetings
iv. Provide the written report to the hPOD TSC and trial co-ordinator

Trial Statistician

The trial statistician will produce (or oversee the production of) the report to the DMC and participate in discussions within the DMC.

Meetings

All members of the DMC shall participate in discussions and voting. Every effort shall be made to reach a unanimous decision. As there are only 3 members of the DMC, all members will be required to participate in all meetings to provide a quorum. All members of the DMC shall disclose competing interests.

The DMC will meet at least annually to review trial progress. Meetings will also be required for interim analysis for the pre-hPOD (dosage) trial after 120, 240 and 360 participants have been accrued and at the end of recruitment to pre-hPOD. Meetings will be face-to-face where possible, with teleconference as a second option. Minutes will be taken by a nominated member of the DMC and kept securely by the Chair.

1. Open sessions

Accumulating information relating to recruitment and data quality will be presented. Members of the Steering Committee may attend the open session.

2. Closed sessions

These will consider efficacy, safety and primary outcome data by treatment group (initially blinded). Only the DMC members will attend the closed session and see the interim analysis. To maintain data integrity, interim analysis will not be

available for review prior to the meeting, and the DMC shall destroy their reports after each meeting. Fresh copies of previous reports will be circulated with the newest report at each meeting.

Recommendations open to the DMC

Possible recommendations may include:

1. No action needed, trial continues as planned
2. Early stopping if there is proof beyond reasonable doubt that:-
    a. Prophylactic oral dextrose gel is either clearly indicated or contraindicated for all babies in the trial or for pre-specified subgroups of participants.

    Or

    b. It is evident that no clear outcome will be obtained.
3. Stopping recruitment within a subgroup
4. Extending recruitment based on actual control group response rates being different from those predicted (rather than on emerging differences between groups).
5. For the pre-hPOD trial – stopping a single arm of the multi-arm trial.
6. Sanctioning and/or proposing protocol changes.

Reporting to the Steering Committee

A letter reporting the DMC's recommendations will be sent to the hPOD Trial Steering Committee and Trial co-ordinator within 2 weeks of each DMC meeting.

Disagreement between DMC and TSC

If the DMC has serious problems or concerns with the hPOD Trial Steering Committee decision a meeting of these groups will be held. The information to be shown at that meeting will depend upon the action proposed and the DMC's concerns. Depending upon the reason for the disagreement, confidential data may have to be revealed to all those attending such a meeting. The meeting will be chaired by an external expert who is not directly involved with the trial and who is agreed upon by both the Chair of the DMC and Chair of the hPOD Trial Steering Committee.

Terms of reference for Safety Monitoring Committee (SMC)

hPOD trial

ACTRN12613000322730

The purpose of this document is to describe the roles and responsibilities of the Safety Monitoring Committee (SMC) for the hPOD trial including the timing, frequency and format of meetings, methods of providing information to and from the SMC and relationships with other committees.

Safety Monitoring Committee

Dr Carl Kuschel (Chair)
Dr Malcolm Battin
Dr Lindsay Mildenhall

Aims

To safeguard the interests of the trial participants and assess the safety of the interventions during the trial.

Relationships

The SMC will receive notification of all adverse events (AE) and serious adverse events (SAE) from the Primary Investigator or a delegated member of the hPOD Trial Steering Committee. The SMC reports to the DMC and also directly to the Steering Committee.

All SAEs will be reported to the SMC by telephone and email within 24 hours of the event on the SAE report form.

All AEs will be complied by the trial co-ordinator and study statistician into a written report and provided to the SMC by email for review after 120, 240 and 360 participants have been accrued and at the end of recruitment to pre-hPOD. It is anticipated that for the multi-centre hPOD trial, AE reports will be provided every 6 months.

The SMC may request further information regarding any SAE or AE event to assist them with their review.

Serious adverse events (SAE)

1. Seizures
2. Neonatal or infant death

Adverse events (AE)

1. Hyperglycaemia (blood glucose concentration > 10 mmol/L)
2. Late hypoglycaemia (blood glucose concentration < 2.6 mmol/L for the first time after 12 hours of age)
3. Delayed feeding (failure to establish breastfeeding without supplements by the end of day three)
4. Systemic sepsis (ANZNN definition)

Duties of the SMC

1. To commence review of all SAEs within 24 hours of receiving report of SAE.
2. To complete review and report to the DMC and, if required the hPOD Trial Steering Committee, within 72 hours of receiving report of SAE.
3. To determine for each SAE reported whether the trial intervention was a causative factor in the SAE occuring.
4. To review each AE report and provide a written report to the DMC, and if required the Steering Committee within 2 weeks of receiving the AE report.

Roles and responsibilities

Safety Committee Chair

The Chair will:

i. Coordinate SMC email correspondence;
ii. Compile members' responses to SAE and AE reports;
iii. Coordinate (together with the trial coordinator) a review of the medical records of cases that require more extensive review;
iv. Provide a written report to the hPOD Trial Steering Committee and DMC;
v. Maintain a record of minutes/reports to be forwarded to the trial coordinator on completion of the trial.

All members

All members of the SMC shall participate in discussions which may be face-to-face or by teleconference. Every effort shall be made to reach a unanimous decision.

Reference document

DAMOCLES Study Group. A proposed charter for clinical trial data monitoring committees: helping them to do their job well. Lancet 2005; 365:711-22