hPOD STUDY Trial Management: ACTRN12614001263684
Terms of Reference document

1. Trial Steering Committee

1.1 Aims

To take overall responsibility for and provide high level academic oversight of the entire study.

1.2 Roles of the Steering Committee

1. Provide academic oversight by advising on study design and protocols and approving major changes as needed.
2. Provide ethics oversight by ensuring all required approvals are in place and up to date, all requirements are complied with, and reports provided as required.
3. Oversee and approve all student projects related to the project (e.g. scope, possible overlaps, etc.).
4. Put in place and maintain a data management framework, including independent data monitoring and independent safety monitoring committees.
5. Oversee data ownership and publications.
6. Oversee funding arrangements for the study, and support funding applications as required.

1.3 Meetings

The Steering Committee will meet approximately once every two months. In alternate months a Management Subcommittee will meet to review operational aspects of the trial. Members will generally not send alternates unless their presence is particularly relevant to the topic of discussion at the meeting.

1.4 Steering Committee Members

Distinguished Professor Jane Harding (Chair)
Professor Caroline Crowther
Dr Jane Alsweiler
Dr Jo Hegarty
Dr Richard Edlin
Mr Greg Gamble (trial statistician)
Other required attendees at Steering Committee meetings: Mrs Kelly Fredell

1.5 Management Subcommittee Members:

Distinguished Professor Jane Harding (Chair)
Dr Jane Alsweiler
Dr Jo Hegarty
Other required attendees at Management Committee meetings: Mrs Kelly Fredell

2. Data Monitoring Committee

2.1 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.

2.2 Relationships

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

2.3 Duties of the DMC

1. To review data prepared by the trial statistician on trial conduct, including updated figures on recruitment, data quality, 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, point 2.6).
3. Advise the hPOD Trial Steering Committee on any additional analyses to be undertaken during the trial.
4. Advise the hPOD Trial Steering Committee on operational procedures affecting recruitment, treatment and follow-up.
5. 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.

2.4 Roles and responsibilities

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

2.5 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.

An initial meeting of the DMC will review the trial protocol and will include an examination of the templates for the DMC reports. No interim analysis is planned. The DMC will meet annually to review trial progress and the reports of the SMC. 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.

2.6 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. Sanctioning and/or proposing protocol changes.

2.6 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.

2.7 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.

2.8 Data Monitoring Committee Membership

Professor Frank Bloomfield (Chair)

Dr Katie Groom

Dr Thomas Lumley (Statistician)

3. Safety Monitoring Committee

3.1 Aims

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

3.2 Relationships

The Safety Monitoring Committee (SMC) will receive notification of all adverse events (AE), serious adverse events (SAE) and protocol deviations from the Primary Investigator or a delegated member of the hPOD Trial Steering Committee. The SMC reports to the Steering Committee and provides reports to the DMC.

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

All AEs will be compiled by the trial co-ordinator and study statistician into a written report and provided to the SMC by email for review every 6 months.

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

3.3 Adverse Events

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)

Other events of concern to the SG may be notified to the SMC e.g. breach of ethical terms such as administration of trial intervention without written consent.

3.4 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 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 Steering Committee within 2 weeks of receiving the AE report.

3.5 Roles and responsibilities

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;
v. Maintain a record of minutes/reports to be forwarded to the trial coordinator on completion of the trial.

3.6 Meetings

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.

3.7 Safety Monitoring Committee Membership

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

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