Study/Trial Full Title: Real Time Continuous Glucose Monitoring in Neonatal Intensive Care

Protocol short title: REACT (RCT)

IRAS ID: 168042

ISRCTN Number: 12793535

ClinicalTrials.gov Identifier (if applicable):

Investigational Medical Device: Real Time Continuous Glucose Monitoring with paper-based algorithm

Chief Investigator: Dr Kathryn Beardsall

Sponsor: Cambridge University Hospitals NHS Foundation Trust and University of Cambridge

Introduction

The role of the Trial Steering Committee (TSC) is to provide overall supervision for the Real Time Continuous Glucose Monitoring in Neonatal Intensive Care on behalf of the Trial Sponsor and the Trial Funder and to ensure that the trial is conducted according to the guidelines for Good Clinical Practice (GCP), Research Governance Framework for Health and Social Care and all relevant regulations and local policies.

The background to this trial, its objectives, assessments, interventions, etc, is described in the trial protocol.

The purpose of this document is to define the roles and responsibilities of the trial TSC and to guide its activities, its relationship with other trial committees, its membership, and the format, purpose and timings of its meetings. The charter also describes the procedures for ensuring confidentiality and proper communication to and from the TSC and an outline of the content of the reports to be provided to the TSC.

Terms of reference

To provide advice, through its Chair, to the Trial Management Group (TMG), the Sponsor and the Trial Funder on all aspects of the trial.

To monitor and supervise the progress of the trial towards its overall objectives, review accrual and results of the trial, adherence to the protocol, patient safety and the consideration of new information of relevance to the trial and the research question.

To ensure that the rights, safety and wellbeing of the trial participants are the most important considerations and should prevail over the interests of science and society.

To ensure that all relevant approvals are obtained before a project begins

To agree proposals for substantial protocol amendments and provide advice to the TMG regarding approvals of such amendments.

To consider the recommendations of Ethics committees, the trial/study DMEC and/or other trial/study committees.

The TSC should inform the TMG if:

There are concerns about the safety of participants

Accrual is too low to provide meaningful results

It is evident that if the study continues it would fail to provide a clear benefit

To terminate the study or further adapt it based on safety and efficacy considerations.

Membership and Primary responsibilities of the TSC

The REACT TSC is a multidisciplinary group composed of the following members who have responsibility for the design, conduct and evaluation of the clinical research project and termination of the trial if deemed necessary. The committee comprises of 71% independent members, 29% non-independent members and 3 attendees and will maintain an approximate 75%/25% split of independent/non-independent members.

Chair: Professor Kate Costeloe (Independent)

Statistician: Professor Tim Cole (Independent)

Clinician: Dr Peter Watkinson (Independent)

Clinician: Dr Andrew Ewer (Independent)

Lay Member: Emma Avery (Independent)

Chief Investigator: Dr Kathryn Beardsall (Non-Independent)

Co-Investigator: Professor David Dunger (Non-Independent)

Senior Clinical Trials Coordinator/CCTU Representative: Dr Paula Kareclas (Attendee)

Trial Statistician: Dr Simon Bond (Attendee)

Study Manager: Catherine Guy (Attendee)

Members of the TMG:

Chief Investigator: Dr Kathryn Beardsall

Co-Investigator: Professor David Dunger

Study Manager: Catherine Guy

Research Nurse: Lynn Thomson

Study Statisticians: Dr Simon Bond and James Howlett (till Feb 2017);

Dr Julia Forman (Feb-Apr 17); Dr Annabel Allison

Senior Data Manager: Beatrice Panataleo

Senior Clinical Trials Coordinator: Dr Paula Kareclas

The Chief Investigator will nominate TSC members to NIHR EME (Funder) Programme Director who will then formally appoint the Chair and independent members.

The responsibility for calling and organising TSC meetings lies with the Chief Investigator in association with the Chair. The Chair assisted by the Chief Investigator is responsible for facilitating the meetings and to summarise discussions.

The TSC membership is for the duration of the trial. If any members leave the TSC, the Chief Investigator in discussion with the Chair should provide replacements and notify EME programme manager of independent members who will need to be formally appointed by the EME programme Director.

Agreements

TSC members should formally register their agreement to be a member of the committee as well as their agreement with the contents of the charter, trial confidentiality and should declare any potential conflicts of interest.

Independent members should complete and return a signed agreement and competing interests form provided at the end of this charter.

Responsibilities

The TSC on behalf of the Sponsor and Funder will have overall responsibility for the design and conduct of the trial and for safeguarding the rights, safety and wellbeing of participants. The TSC has the authority to suspend or terminate the Trial. The DMEC can make recommendations for such action to the TSC but the decision lies with the TSC. Responsibilities of the TSC to include:

Reviewing selection/recruitment/retention of participants and their management

Finalising and reviewing study protocol and other study documentation.

Determine if amendments to the protocol or changes to study conduct are required and deciding on changes to these and to study conduct in general. Any changes to trial documentation or conduct must be notified to the TSC.

Reviewing adherence to the protocol by Investigators and participants

Assessing the impact and relevance of external evidence

Assessing integrity and completeness of data collected

Monitoring the overall conduct of the trial, ensuring that it follows the standards set out in the guidelines of GCP, assessing the safety and efficacy of the interventions, recruitment figures and completion of trial assessments.

Reviewing, commenting and making decisions on extension requests.

Reviewing the recommendations of the DMEC and/or other study committees and suggesting appropriate action to the TMG

Monitoring the progress of study/trial and deciding on appropriate action in order to maximise the chances of completing it within the agreed timelines.

Considering new information relevant to the study e.g. results from other studies that may have a bearing to the conduct of the study and deciding on appropriate action.

Endorsing the annual report to the funder

The TSC may terminate the trial or modify the trial design in the event of a clear outcome derived from accumulating data or on the basis of information available from other sources or on safety grounds.

The TSC should be available to provide independent advice as required not just when meetings are scheduled.

The TSC should maintain confidentiality of all information it receives.

Members should not discuss confidential issues from their involvement in the study until the primary results have been published.

Role of the TSC Chair

Arrange the first meeting of the TSC with the assistance of the CI to agree contents of charter and set up schedule of meetings prior to recruitment of participants

Establish clear reporting lines – to the Funder, Sponsor etc

Become familiar with the role of the DMEC

Provide an independent, experienced opinion if conflicts arise between the needs of the research team, the Funder, the Sponsor and/or any other agencies

Leading the TSC to provide regular, impartial oversight of the trial, especially to identify and pre-empt problems

Ensuring that changes to the protocol are debated and endorsed by other members of the TSC

For decisions to be made, at least 2 independent members of the TSC should be present (including the chair) and a non-independent member (CI or Co-Investigator). Only members of the committee (not attendees) can vote.

TSC meetings

The responsibility for calling and organising a TSC meeting lies with the CI in association with the TSC Chair.

The study manager will organise these on behalf of the CI

Meetings will be in person and by teleconference

All TSC members will be provided with study documents (e.g. protocol, proposed statistical analysis plan (SAP), PIS, CRF etc) and the TSC report prior to the meeting.

The first TSC meeting should ideally be held face-to-face to discuss, revise and finalise the terms of reference, agree the content of the TSC charter and sign any declaration, and agree the frequency of the meetings.

It is anticipated that TSC meetings will be held every 6-8 months depending on progress of recruitment

Meetings can also be held at any time at the request of the CI or TSC chair

The final TSC meeting will be arranged when target recruitment is completed, all data collected and cleaned, and the database is locked. This final meeting will be held to discuss final/completed data and interpretation, and publication timeless. If the study is terminated prematurely, no final study meeting is required.

Attendance

Every effort will be made to ensure that all TSC members can attend the meetings. The study manager or delegate should try and find a date that enables this. The CI must try to attend all meetings, especially if major actions are expected.

Two independent TSC members (including the Chair) and a non-independent member (CI or Co-Investigator) need to be present for a meeting to take place.

If the TSC is considering major actions the TSC Chair should communicate with absent members, including the CI, as soon after the meeting as possible to determine whether they all agree. If there is disagreement amongst absent members a further meeting should be arranged with the full TSC.

Reporting

The DMEC will report directly to the TSC and submit regular reports to the TSC Chair.

Prior to a TSC meeting a report will be prepared by the TMG with input from the study manager, data manager and statistician and circulated to TSC members at least a week before the meeting.

On consideration of the information presented at these meetings, the TSC should provide recommendations of appropriate action in writing to the TMG who will be responsible for implementing any actions. The TSC may also provide feedback to the IDMEC and where appropriate to the Sponsor/Funder.

Minutes of the meeting including key points and actions will be prepared by the study manager. These minutes will describe the proceedings and include the recommendations of the TSC. All members of the TSC must agree the minutes and these will be signed off by the TSC Chair on behalf of all members. Minutes will be circulated to all TSC members, the TMG, the Sponsor and, if appropriate, the Trial Funder. Approved Minutes will be filed in the Trial Master File.

Decisions and recommendations by the TSC should be unanimous if not a vote may be taken. The role of the Chair is to summarise discussions and encourage consensus. Therefore, it is best for the chair to give her opinion last. It is important that the implications (ethical, statistical, practical, and financial) for the trial be considered before any decision is made.

Contents of the TSC Reports

An outline of the contents of the TSC report is given below:

Study synopsis in addition to current available evidence

Statistical consideration and design

Major protocol amendments

Patient screening

Eligibility violations

Protocol violations by investigators

Study accrual by month/total

Completeness and quality of data collected/CRF return

Data quality/monitoring

CRF return, entry into database

Baseline characteristics

Demographics

Disease characteristics

Safety reporting

Any matters affecting the trial

Latest DMEC report and DMEC recommendations

Conflicts of interest

TSC members should not have any apparent financial, scientific or intellectual conflict of interest that could prevent them from objectively reviewing the study protocol, interim and final data and giving advice to the TMG. TSC members should disclose to the Chair any other conflicts they consider relevant. Any members who develop significant conflicts of interest during the course of the trial should resign from the TSC.

Publication

Manuscripts that arise from the trial will be shared with the TSC and members will be able to comment. The TSC members and their affiliations will be acknowledged in reports of the trial.

References:

1. CCTU/GD018

2. MRC Guidelines for GCP in clinical trials (1998)

3. MHRA GCP Guide (2012)

Annexe 1

Agreement and competing interests form for independent members of the Real Time Continuous Glucose Monitoring in Neonatal Intensive Care (REACT RCT) Trial Steering Committee.

Please complete the following document and return to:

Study Manager
REACT RCT Trial
University Department of Paediatrics
University of Cambridge
Box 116, Level 8
Cambridge Biomedical Campus
Hills Road
Cambridge CB2 0QQ

☐ I have read and understood the TSC charter version 1.0 dated 11 December 2014

☐ I agree to join the TSC for this trial as an independent member

☐ I agree to treat all sensitive trial data and discussions confidential

The avoidance of any perception that members of the TSC may be biased in some fashion is important for the credibility of the decisions made by the TSC and for the integrity of the trial. Possible competing interest should be disclosed via the trials office. In many cases simple disclosure up front should be sufficient. Otherwise, the (potential) TSC member should remove the conflict or stop participating in the TSC. Table 1 lists potential competing interests:

Table 1: Potential competing interests for independent members

1. Stock ownership in any commercial companies involved.
2. Stock transaction in any commercial company involved (if previously holding stock)
3. Consulting arrangements with the Sponsor
4. Frequent speaking engagements on behalf of the intervention
5. Career tied up in a product or technique assessed by the trial
6. Hand-on participation in the trial
7. Involvement in the running of the trial
8. Emotional involvement in the trial
9. Intellectual conflict e.g. strong prior belief in the trial's experimental arm
10. Involvement in regulatory issues relevant to the trial procedures
11. Investment (financial or intellectual) in competing products
12. Involvement in the publication

☐ **NO,** I have no competing interests to declare

☐ **YES,** I have competing interests to declare (please detail below)

_____

_____

_____

Name: _____

Signed:_____ Date: _____
algorithm

Chief Investigator: Dr Kathryn Beardsall

Sponsor: Cambridge University Hospitals NHS Foundation Trust and University of Cambridge