Abdominal massage for neurogenic bowel dysfunction in people with multiple sclerosis

DATA MONITORING AND ETHICS COMMITTEE CHARTER

Funder number	12/127/12
REC number	14/WS/0111
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Authorised by:

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1.Introduction

The AMBER trial is funded by the NIHR HTA. Research Ethics Committee approval has been given by West of Scotland (ref. no. 14/WS/0111). The sponsors of the study are Glasgow Caledonian University. AMBER trial has been registered on Current Controlled Trials (www.controlled-trials.com, ISRCTN). The Trial Office is located in Glasgow at the NMHAP Research Unit, Glasgow Caledonian University, Glasgow.

1.1.*Trial Objectives*

AMBER is a randomised controlled clinical trial to compare intervention versus no intervention in clinical practice.

1.2.*Scope*

The purpose of the document is to describe the roles and responsibilities of the independent DMEC for the AMBER trial, including the timing of meetings, methods of providing information to and from the DMEC, frequency and format of meetings, statistical issues and relationships with other committees.

1.3.*Facilitation*

The AMBER trial manager will be nominated as a facilitator for the committee. The Facilitator will be responsible for the organisation of the meetings. A summary of each DMEC meeting will be sent to the trial manager for information.

2.Roles and responsibilities

2.1.*Aims of DMEC*

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.*Terms of reference*

The role of the DMEC is to receive and review information on the progress of recruitment and accruing data of this trial, and to provide advice to the Trial Steering Committee (TSC).
The DMEC should inform the Chair of the TSC if, in their view:

i) The results are likely to convince a broad range of clinicians, including those supporting the trial and the general clinical community, that, on balance, one trial arm is clearly indicated or contraindicated for all participants or particular category of participants, and there was a reasonable expectation that this new evidence would materially influence patient management.
ii) There are significant concerns about patient safety in either arm of the trial.

2.3.*Specific roles of DMEC*

The DMEC's role will include, but not be restricted to, the following:

- monitor recruitment rate and loss to follow up rate
- assess data quality, including completeness of data collection
- define the timing and nature or interim analyses required
- monitor evidence for treatment differences in the main efficacy outcome measures
- monitor evidence for treatment harm (eg SAEs, deaths, complication rates)
- decide whether to recommend that the trial continues to recruit participants or whether recruitment should be terminated either for everyone or for some treatment groups and/or some participant subgroups
- suggest additional data analyses
- monitor planned samples size assumptions
- monitor continuing appropriateness of patient information
- assess the impact and relevance of external evidence

6. Organisation of meetings

6.1. *Frequency*

The DMEC will meet approximately yearly or more often if the DMEC considers it necessary to do so.

6.2. *Attendance*

Effort will be made to ensure that all members can attend. The CI and trial statistician will attend at the request of the Chair. Members who cannot attend in person should be encouraged to participate by teleconference. If, at short notice, any DMEC members cannot attend then the DMEC may still meet if at least two independent members, including the Chair (unless otherwise agreed), will be present. If the DMEC is considering a major action after such a meeting the DMEC Chair should communicate with the absent members, as soon after the meeting as possible to check they agree. If they do not, a further teleconference should be arranged with the full DMEC.

The meeting report will be circulated at least one week before the meeting in order to enable DMEC members who will not be able to attend the meeting to pass comments for consideration during the discussions at the meeting to the DMEC Chair.

6.3. *Independent members who fail to attend meetings*

If an independent member does not attend a meeting or provide comments when requested between meetings, it should be ensured that the independent member is available for the next meeting. If an independent member does not attend the next meeting or provide comments when next requested, they should be asked if they wish to remain part of the DMEC. If an independent member does not attend a third meeting, strong consideration should be given to replacing this member.

6.4. *Resignation and replacement of independent members due to change in circumstances*

If an independent Committee member's circumstances change (e.g. if he/she moves job to the same institution as the CI) he/she would resign from the committee. A replacement independent member would be identified and appointed.

7.Trial documentation and procedures to ensure confidentiality and proper communication

7.1. *Material to be considered during meetings*

The statistician will provide a report to the DMEC including data to be specified by the DMEC and a short report regarding recruitment progress and any management issues will be prepared by the central coordinating office. This will report on accrual against time and target and any matters affecting the trial.

As a minimum the following information will be reviewed:

- Recruitment to time and target
- A list of reported SAEs
- Any new, relevant or possibly relevant publications identified by the Trial Office
- Interim analyses as specified by the DMEC

7.2. *Accumulating data*

The accumulating study data by arm and interim analyses will be confidential. These will be available to the DMEC. The DMEC will make recommendations in writing to the TSC based on the interim data.

7.3. *Retention of papers after the meeting*

The Chair of DMEC will keep a central record of all minutes, reports and correspondence by the DMEC. Summary reports will be sent to the TSC and Trial office, with any appropriate recommendations. DMEC members will be expected to securely and confidentially retain minutes and reports until the end of the trial. After completion of the trial, confidential DMEC

documents will be archived centrally with the other trial documentation. DMEC member will then delete, or destroy copies of the reports to and from the DMEC, agenda and minutes, as well of copies of communications between meetings. All documentation should be considered confidential.

8. Decision making

8.1 *Possible DMEC recommendations*

Based on review of interim analyses by the DMEC, the possible recommendations to the DMEC could include:-

- No action needed, trial continues as planned
- Early stopping due, for example, to clear benefit or harm of a treatment, or external evidence
- Stopping recruitment within a subgroup
- Requesting an additional interim analysis

The DMEC may recommend unblinding of the TSC to outcome data if a recommendation to stop the trial or recruitment to a subgroup is made.

8.2. *Analysis*

The DMEC should review and agree any interim analysis plan at their first meeting.

8.3. *DMEC decision making methods*

The role of the Chair is to summarise discussions and encourage consensus; therefore, it may be best for the Chair to give their own opinion last. It is important that the implications (e.g. ethical, statistical, practical and financial) for the trial be considered before any decision is made.

8.3. *When the DMEC is quorate*

At least two independent members of the DMEC should be present including the Chair, plus a representative of the trials unit and, if major action is to be considered, the CI.

8.4. *Voting rights*

If a vote is required, all independent members will have a full vote. In addition the CI, or appropriate deputy if CI is unable to attend the meeting, may also vote. In the event of a tied vote, the independent DMEC Chair will have the casting vote.

9. Reporting

9.1 *Communication of DMEC recommendations*

Reports of meetings will be sent to the Chair of the Trial Steering Committee within three weeks of each meeting. A copy will be lodged with the trial office, and also sent to the Chief Investigator. Minutes of the meetings will be kept and signed off by the Chair after each meeting.

A meeting of the TSC will be convened within a few weeks of receipt of the report, to discuss recommendations made by the DMEC. A copy of the minutes of that meeting will be sent back to the Chair of the DMEC.

9.2. *Conflict resolution with other study Committees*

If the DMEC has serious problems or concerns with the TSC decision made in response to the DMEC report, a meeting of both committees should be held. The information to be shown would depend upon the action proposed and the DMEC's concerns. Depending on the reason for the disagreement confidential data will often have to be revealed to all those attending such a meeting.

The meeting would be chaired by a senior member of the central Trial Office or an external expert who is not directly involved with the trial.

10. After the trial

10.1 *Publication of results*

At conclusion of the trial, a copy of the final analysis will be proviced to the DMEC chair. He may convene a final meeting of the committee to review this. Names and affiliations of the DMEC members will be included in the trial protocol and the final report. The details of the trial conduct, the results, and the members' involvement in the trial shall remain confidential until 12 months after publication of the final report.

There may be a meeting to allow the DMEC to discuss the final data with the writing committee to give advice about data interpretation.

10.2. *DMEC acknowledgement in publications*

DMEC members will be named and their affiliations listed in the main report, unless they explicitly request otherwise.

Annexe 1: Agreement and competing interests form for independent members

<u>AMBER Data Monitoring and Ethics Committee:</u> Agreement to join the AMBER Trial Data Monitoring and Ethics Committee as an independent member and disclosure of potential competing interests.

Please complete the following document and return to the DMEC Facilitator
(Please initial box to agree)

☐ I have read and understood the DMEC Charter version 1.0, 25th August 2014.

☐ I agree to join the Data Monitoring Ethics Committee for this trial as an independent member

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

The avoidance of any perception that independent members of a DMEC may be biased in some fashion is important for the credibility of the decisions made by the DMEC and for the integrity of the trial.

Potential competing interests should be disclosed via the DMEC facilitator. In many cases simple disclosure up front should be sufficient. Otherwise, the (potential) independent DMEC member should remove the conflict or stop participating in the DMEC. **Table 1** lists potential competing interests.

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

☐ **No,** I have no potential competing interests to declare

Please provide details of any potential competing interests:

_____

_____

Name: _____

Signed: _____ Date: _____

Table 1: Potential competing interests for independent members

Stock ownership in any commercial companies involved
Stock transaction in any commercial company involved (if previously holding stock)
Consulting arrangements with the Sponsor/Funder
Ongoing advisory role to a company providing drugs and devices to the trial
Frequent speaking engagements on behalf of the intervention
Career tied up in a product or technique assessed by trial
Hands-on participation in the trial
Involvement in the running of the trial
Emotional involvement in the trial
Intellectual conflict e.g. strong prior belief in the trial's experimental arm
Involvement in regulatory issues relevant to the trial procedures
Investment (financial or intellectual) or career tied up in competing products
Involvement in the writing up of the main trial results in the form of authorship

Note: This DMEC charter was developed using MRC CTU template DMEC Charter version 2.01, 13-Mar-2006