FLuid Optimisation in Emergency LAparotomy

(FLO-ELA) Trial

Data Monitoring and Ethics Committee (DMEC) Charter

Version 2.0

31st May 2017

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1. Introduction

Main sponsor	University Hospital of Southampton (UHS)
Funder	NIHR Health Technology Assessment programme
Study coordination	Pragmatic Clinical Trials Unit (PCTU)
ISRCTN reference	14729158

OBJECTIVE

To establish whether minimally invasive cardiac output monitoring to guide protocolised administration of intra-venous fluid during and for up to six hours after major emergency bowel surgery will reduce the number of patients who die within 90 days of randomisation.

DESIGN

Open, multi-centre, randomised controlled trial

POPULATION

Patients aged 50 years and over undergoing an expedited, urgent or emergency major abdominal procedure on the gastrointestinal tract eligible for inclusion within NELA.
The trial will recruit 7646 patients (3823 per arm).

EXCLUSION CRITERIA

Refusal of patient consent, clinician refusal, abdominal procedure outside the scope of NELA, previous enrolment in the FLO-ELA trial, previous inclusion in the NELA audit within the same hospital admission, current participation in another clinical trial of a treatment with a similar biological mechanism.

INTERVENTION

Cardiac output monitoring to guide protocolised administration of intra-venous fluid

DURATION

57 months

PRIMARY OUTCOME

Mortality 90 days after trial randomisation

SECONDARY OUTCOMES

One-year mortality; length of stay in hospital and intensive care; hospital readmission within 90 days; cost effectiveness.

2. Membership of the DMEC

Independent Members			
Name	**Position in DMEC**	**Job Title**	**Institution**
Prof. Ian Roberts	Chair	Professor of Epidemiology & Public Heath	London School of Hygiene & Tropical Medicine
Prof. Danny McAuley	Independent Member	Professor of Intensive Care Medicine	Northern Ireland Clinical Trials Unit
Dr Tim Morris	Statistician	Statistician	University College London

Observers*			
Name	**Role in Trial**	**Job Title**	**Institution**
Dr Mark Edwards	Chief Investigator	Consultant in Anaesthesia and Perioperative Medicine	University Hospital of Southampton
Prof. Rupert Pearse	Senior Co-Investigator	NIHR Research Professor & Consultant in Intensive Care Medicine	Royal London Hospital
Prof. Mike Grocott	Senior Co-Investigator	Professor of Anaesthesia and Intensive Care	University Hospital of Southampton

**please note: this list is not exhaustive. Observers will be invited to attend open meetings as needed, depending on the agenda (please see 5. DMEC Meetings).*

3. Responsibilities of the DMEC

- The role of the Data Monitoring Committee (DMEC) is to safeguard the interests of trial participants, assess the safety and efficacy of the interventions during the trial, and monitor the overall conduct of the clinical trial. Day to day management of the trial is the responsibility of the investigators. A separate Trial Management Group (TMG) has been convened for this purpose.
- The DMEC should receive and review the progress and accruing data of this trial and provide advice on the conduct of the trial to the Trial Steering Committee.
- The DMEC should inform the Chair of the steering committee if, in their view:
    i. there is overwhelming evidence that is likely to convince a broad range of clinicians, including those supporting the trial and the general clinical community, that one trial arm is clearly indicated or contraindicated, and

there was a reasonable expectation that this new evidence would materially influence patient management; or

ii. it becomes evident that no clear outcome would be obtained

- Specific roles of the DMEC include:
  - assess data quality, including completeness (and by so doing encourage collection of high quality data)
  - monitor recruitment figures and losses to follow-up
  - monitor compliance with the protocol
  - monitor evidence for treatment differences in the main efficacy outcome measures
  - monitor evidence for treatment harm by reviewing SAEs
  - 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
  - monitor compliance with previous DMEC recommendations
  - assess the impact and relevance of external evidence
  - to provide a letter of agreement to action, post review of any protocol modifications (as initiated by the Investigator and TSC).

4. CI/Trial Team Responsibilities

- Notify the DMEC of any emerging research or safety data relevant to the trial.

5. DMEC Member Indemnity

- University Hospital Southampton NHS Foundation Trust (UHS) is the Sponsor for the FLO-ELA trial and as such assumes all responsibility and understands it is fully accountable for the management, monitoring and conduct of the study in accordance with the role of the Sponsor as detailed in the Research Governance Framework. UHS confirms that the members of the DMEC shall have no liability with respect to the conduct of the FLO-ELA trial and all such liability shall be borne by UHS as Sponsor.
- This indemnity agreement will be reflected in a signed letter from the sponsor to each voting member of the DMEC.

6. DMEC reports

- Reports will be prepared by an independent statistician under instruction from the trial statistician.
- The reports will be divided into 'Open' and 'Closed', with the following content:
  - Open Reports – to be viewed by all members and observers
    - Recruitment figures (including screening and retention data)
    - Number allocated to each treatment arm
    - Missing outcome data
  - Closed Reports – to be viewed by only the Independent Members
    - Outcome data by treatment group
    - Safety Data by treatment group
- The reports, where applicable, will be circulated at least a week before each DMEC meeting.

7. DMEC Meetings

Planned Meetings:

- The responsibility for calling and organising DMEC meetings lies with the Chief Investigator, in association with the Chair. The DMEC will plan to meet every 6 months. Except where all members agree that a 6 monthly meeting is not necessary, in which case the committee must meet at least once a year.
- If a member misses 3 meetings in a row, the remaining members will nominate a new member to replace them.
- DMEC meetings should occur before TSC meetings, to allow the TSC to view DMEC recommendations.
- The meetings will be divided into 'Open' and 'Closed' sections, this will be reflected in the agenda. Only Independent Members will attend the 'Closed' section.
- The agenda will be drafted by the Trial Management Group (TMG) and agreed by the chair.
- DMEC meetings will be arranged to try and ensure all members can attend. Members who cannot attend in person will be encouraged to attend by teleconference.
- The observers are not members of the DMEC but may be invited to all or part of the meeting to provide expert input.

Minutes:

- Minutes of the open section of the meetings will be written by the Trial Manager and approved by the Chief Investigator and the DMEC Chair.
- The minutes will be circulated to members of the DMEC and any observers present.

- The minutes will be filed and stored in the Trial Master File (TMF).
- DMEC members would be expected to securely store copies of the reports to and from the DMEC, agenda and minutes, as well as copies of communications between meetings. All documentation should be considered confidential.
  No formal minutes will be produced for the closed section of the meetings. Instead, a letter to the TSC will be produced, with recommendations to continue or discontinue the trial.

Recommendations:

- Major decisions should involve all DMEC members
- Every effort should be made to achieve consensus. The role of the Chair is to summarise discussions and encourage consensus.
- If a consensus cannot be reached this should be recorded and, if necessary, reported to the TSC.
- The Chair, Chief Investigator and Trial Manager are responsible for reporting DMEC recommendations to the TSC, relevant bodies and groups.
- In cases where the DMEC have a serious concern about safety, and the TSC disagrees with the DMEC's recommendation, a joint meeting will be called. The meeting should be chaired by an independent senior member of a Clinical Trials Unit and should involve a sponsor's representative.

DMEC Members Signature Page

Do you have any conflicts of interest? YES/NO (*if yes please detail them below*):

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I confirm that I have read this Charter; I understand it and I will work according to it. I will also work consistently with the ethical principles according to ICH Guidelines of Good Clinical Practice and the applicable laws and regulations.

Name	
Position	
Signature	
Date	

DMEC Members Confidentiality Agreement

All members of a DMEC convened to oversee the conduct of a study must recognise, confirm their commitment to, and comply with the principles of confidentiality in relation to all study data made available to them to discharge their responsibilities as members of the trial steering committee. This includes:

- Non-disclosure of the protocol, protocol amendments, data, minutes of meetings or any other documentation circulated in relation to the operation of the DMEC to unauthorised individuals
- Ensuring that all documents relating to the operation of the DMEC are held securely and are not accessible to others
- Ensuring that all documents in their possession are destroyed at the end of the study

I confirm that as a member of the DMEC for the study entitled **FLuid Optimisation in Emergency LAparotomy (FLO-ELA) Trial**, I will abide by the principles of confidentiality outlined above.

Name	
Position	
Signature	
Date	