Trial Monitoring Plan

Optimisation of Perioperative Cardiovascular Management to Improve Surgical Outcome II (OPTIMISE II) Trial

Chief Investigator: Professor Rupert Pearse

Lead Site: Barts Health NHS Trust

Number of Sites: 50

Non-CTIMP study

Monitoring plan version	1.0
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Role	Printed name and job title	Signature
Author	Nazia Uddin (QA Officer)	
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Chief Investigator	Professor Rupert Pearse	

Document History

Version	Date	Section	Reason for Change
1.0			N/A

Audit : TMF will be audited annually by the PCTU QA manager/officer
Monitoring will be conducted twice per study site by the PCTU trial monitor

Trial Monitoring Plan

1.0 Scope:

All trials supported by the Pragmatic Clinical Trials Unit (PCTU) will be risk assessed (see PCTU SOP/TP_04 Risk Assessment) to determine the level and frequency of monitoring appropriate for the study. All clinical trials of investigational medicinal products (CTIMPs) will be risk assessed and monitored by the PCTU monitor/s and subject to regular audits by the PCTU Quality Assurance (QA) manager, to ensure compliance with the Medicines for Human Use (Clinical Trials) Regulations 2004, the Research Governance Framework (2008), ICH-GCP and the requirements of the sponsor and PCTU. The Trial Monitoring Plan (TMP) will outline the plan for study start-up and site initiation, level and frequency of monitoring for the study, detail all relevant contacts and outline the procedure for trial close out.

Definition of Abbreviations

CI	Chief Investigator
CRF	Case Report Form
GCP	Good Clinical Practice
ISF	Investigator Site File
PCTU	Pragmatic Clinical Trials Unit
QA	Quality Assurance
QC	Quality Control
REC	Research Ethics Committee
SAE	Serious Adverse Event
SDV	Source Document Verification
SOP	Standard Operating Procedures
Subject	An individual who takes part in a clinical trial
TMF	Trial Master File
TMP	Trial Monitoring Plan

Trial Monitoring Plan

Contents

1. Trial Summary

The study is a multinational, open-label, multicentre randomised controlled trial entitled 'Optimisation of Perioperative Cardiovascular Management to Improve Surgical Outcome II (OPTIMISE II) Trial'. The primary objective is to evaluate whether cardiac output monitoring guided administration of IV fluids and low dose inotrope infusion in patients undergoing major elective gastrointestinal surgery results in reduced incidence of post-operative infection and reduced mortality and morbidity in this patient group and it is planned to recruit 2502 number of subjects into the study. This is a multicentre study with sites approximately 50 subjects per site. Approximately 15 sites are in the UK, 35 sites are outside of the UK. The CRF for the study will be paper based and the database used will be a bespoke web based clinical trials data management system with in-built audit trail and validation. The database for the study will be provided by the Data Manager at the Critical Care Unit. Subject numbers will be allocated by the randomisation system. Data entry and query responsibilities will be provided by the study team. Randomisation will be via web based randomisation system housed within the trial database.

The study DMEC and TSC will meet every 6/12 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.

2. Risk Assessment

This study was risk assessed by the PCTU QA manager and the Sponsor. The PCTU risk assessment was conducted in accordance with PCTU SOP TP 04: Risk Assessment with the result that the risk level for the study is low.

It has been agreed by the Sponsor, PCTU and CI that responsibility for audit & monitoring this study will be delegated to the PCTU.

3. Audit/Monitoring Plan:

Though this study has been determined to be low risk by the PCTU, considering the study intervention design, this study will be audited annually and each site will have two on-site monitoring visits conducted within 6 months of the site recruiting its first participant and the second visit will be planned one year after the first monitoring visit. If appropriate, additional monitoring visits may be organised to address specific trial related problems at a site. This will allow the monitor to review data entry at a site outside the above timelines. 100% Source Data Verification (SDV) will be carried out for the primary outcomes at 30 day follow-up for up to 10 patients at each visit.

The annual audit will be conducted by the PCTU QA team in London and UK sites will be monitored by the PCTU Monitor. The PCTU and CI have agreed each site in countries outside the UK will have monitoring visits conducted by the following:

Country	Monitored by
Australia	CRO/ National coordinator
Germany	National coordinator/ Member of R.P team
Spain	PCTU Monitor/ Member of R.P team
Sweden	PCTU Monitor/ Member of R.P team
US	National coordinator
Canada	National coordinator

For the international sites one of the following strategies will be used: PCTU Monitor/ Monitor from Rupert Pearse's (R.P) team/ National Coordinator to provide the monitoring. This will be discussed on a site by site basis and the monitoring plan will be updated accordingly.

All audit & monitoring will be done in accordance with PCTU SOP_QA 02 (QA and QC system) and PCTU SOP_QA 04 (Monitoring of PCTU supported research projects).

4. Trial Start Up

4.1. PCTU, Study Team and Other Relevant Trial Contacts

Job Title	Name	Contact Details
PCTU QA Manager	Anitha Manivannan	a.manivannan@qmul.ac.uk
PCTU Trial monitor	Jeanette Hansen	J.hansen@qmul.ac.uk
PCTU Data Manager	Mike Waring	m.r.waring@qmul.ac.uk
Chief Investigator	Professor Rupert Pearse	r.pearse@qmul.ac.uk
Co-Investigator	Dr Mark Edwards	mark.edwards2@uhs.nhs.uk>
Trial Manager/Coordinator	Priyanthi Dias	p.dias@qmul.ac.uk
Senior Trial Manager	Ann Thomson	ann.thomson@qmul.ac.uk
Sponsor RG & GCP Manager	Marie-Claire Rickard	m.rickard@qmul.ac.uk

4.2. List of relevant PCTU and Trial specific SOPs

All PCTU SOPs relevant to this study will be followed and following trial specific SOPs will also be utilised during the study:

SOP Title	SOP Number	Author
Management of intervention group patients, version 1.0	SOP 001	Mark Edwards & Rupert Pearse
Management of control group patients, version	SOP 002	Mark Edwards & Rupert

1.0		Pearse
Delegation of trial duties	SOP 003	
Patient screening and informed consent procedures	SOP 004	
Infection follow-up	SOP 005	
Morbidity follow-up	SOP 006	
Data collection manual	SOP 007	
SAE reporting	SOP 008	

4.3. Approvals

The chief investigator (in liaison with the sponsor) will have responsibility for obtaining all relevant approvals for the study prior to start-up; these include REC (UK), REC equivalent in other countries and local R&D approvals. All correspondence prior to trial commencement with the sponsor, host sites, and regulators should be documented and filed in the appropriate ISF, TMF, and / or R&D files.

4.4. Multi-Site Studies

The CI will approach and select all other sites to take part in the study. The coordinating centre will facilitate application for the relevant approvals by individual sites. All pre-trial contacts will be documented and filed as for approvals (see section 4.1). The sponsor will facilitate the set up and approval of all site agreements (contracts).

4.5. Essential Pre-Trial Documents

The study cannot commence at any site until all necessary approvals have been granted and all essential documentation is in place and filed in the TMF/ISF. A site initiation visit (SIV) will be conducted by the trial manager and/or co-ordinator and the coordinating study team, to ensure that all relevant approvals and documentation is in place at site.

5. Trial Initiation

All sites will be initiated by on-site visit by the trial manager and/or trial coordinator. The following must be discussed, agreed and documented at the initiation visit:

- All relevant approvals and agreements are in place for the study and the site
- Signed protocol agreement
- Study data management procedures
- Study randomisation procedures
- ISF and essential documentation are in place at site
- Completed delegation log

- Training in study protocol and study SOPs
- Safety reporting requirements and responsibilities
- Supply of materials/equipment to site
- Maintenance of the ISF
- Trial monitoring plan
- Archiving at site

The trial co-ordinator is to ensure that a log detailing attendance at the meeting, date of site visit and all initiation documentation is present in ISF for future reference.

6. Trial Closure

Site close out will be performed on-site/by teleconference after all data queries have been resolved. The trial manager will confirm with the QA manager when the database has been locked. The close out will then be performed by the trial coordinator in accordance with PCTU/TC_01 SOP on trial close out.