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Our ref: 2020-KEP-420

Professors Haleema Shakur-Still and Ian Roberts
DPH/EPH
LSHTM

9 April 2020

Dear Haleema and Ian,

Re: Aspirin, losartan and simvastatin in hospitalised COVID-19 patients: a multinational randomised open-label factorial trial (CRASH-19)

As the authorised representative for the London School of Hygiene & Tropical Medicine (LSHTM), I can confirm that LSHTM will act as the identified Research Sponsor, the organisation that takes responsibility for the initiation, management, and/or financing of a clinical trial, for the above titled project. I can confirm that the research proposal has been reviewed, assessed and registered by the Research Governance and Integrity Office.

It is the Chief Investigator's responsibility to ensure that members of the research team comply with all regulations applicable to the performance of the project, including, but not limited to: Good Clinical Practice (the ICH GCP R2 (2016) guidelines are recommended as internationally recognised), the Declaration of Helsinki (2013), and for projects conducted in the UK: the Medicines for Human Use (Clinical Trials) Regulations (2004), the Data Protection Act (2018), the Human Tissue Act (2004), and the UK Policy Framework for Health and Social Care Research (2017).

LSHTM carries Clinical Trial/Non-Negligent Harm Insurance and Medical Malpractice Insurance applicable to this study. The RGIO confirms that this study does not fall under any exclusion criteria in the policy:

Insurer	Newline
Policies	FI08161119 (Renewable annually in June): £10 million pounds sterling (any one claim and in the annual aggregate)
No. of Participants	10,000

The Non-Negligent harm policy is worldwide, with the exception of the United States and Canada. The policy is subject to terms, conditions and exceptions.

LSHTM Sponsorship is conditional on the project receiving applicable ethical and regulatory approval, complying with LSHTM / MRC Unit at LSHTM policies and procedures, as well as successful contract and agreement negotiations before the study commences.

A copy of the ethics and regulatory approval letters **must** be sent to the Research Governance and Integrity Office prior to the study commencing. Sponsorship is dependent on obtaining local approval for all sites where the research is being conducted. It is recommended that all members of the study team attend Good Clinical Practice (GCP) training every two years.

Yours sincerely,

Patricia Henley
Head of Research Governance and Integrity

POLICY DOCUMENT COVERING SPONSORSHIP

The main responsibilities of Sponsor delegated to the Chief/Principal investigator are:

(i) Authorisations

- Obtain favourable opinion from ethics committee
- Request clinical trial authorisation (CTA) from Regulatory Authority (as required)
- Study submitted to public database (eg www.clinicaltrials.gov)
- Give notice of amendments to the protocol
- Provide annual reports to all relevant authorities including the LSHTM REC
- Give notice a trial has ended and ensure results are added to a public register

(ii) Good Clinical Practice and conduct (GCP)

- Put and keep in place arrangements to adhere to GCP
- Ensure all members of study team receive appropriate training in GCP, clinical trial protocol and applicable procedures
- Conduct the study in accordance with the approved research protocol *except where necessary to eliminate an immediate hazard(s)*
- Compliance with all LSHTM / MRC at LSHTM Units Standard Operating Procedures (SOPs)
- Ensure the RGIO is informed of any potential serious breaches of GCP and/or the protocol

(iii) Pharmacovigilance

- Defined process for continued safety monitoring of IMP in study
- Keep records of all adverse events/ adverse reactions
- Report serious adverse events/ serious adverse reactions at least annually (or more frequently, as required), typically via a Developmental Safety Update Report (DSUR)
- Ensure recording and prompt reporting of suspected unexpected serious adverse reactions (SUSARs) to all regulatory authorities, as required
- Ensure all investigators on the trial are informed of SUSARs

(iv) Trial Management

- Responsibility to maintain a Trial Master File and Investigator Site File containing the essential documents and to make the site file available for audit and inspection
- Ensure appropriate Quality Control (monitoring) mechanisms for study based on risk assessment
- Provide medical expertise for all participants enrolled in trial
- Ensure data collected and reported are accurate, complete and identifiable at source; and that record keeping and data transfer procedures adhere to relevant Data Protection laws.
- Ensure appropriate selection of investigator(s) and members of the trial team with relevant written delegation of responsibilities
- Provide record access for QA/QC and regulatory inspections
- Appropriate study design and statistical analysis for study
- Responsibility to make the necessary provision for archiving essential documents

(v) Investigational Medicinal Product (IMP)

- Ensure IMP are available to participants free of charge
- Liaise with Pharmacy/or other relevant appropriate personnel to document the supply, handling and accountability of all trial drugs per regulations and SOPs
- Information on IMP kept up to date
- Manufacturing, Packaging, Labelling, and Coding of IMP per SOPs

The main responsibilities retained by the Sponsor are:

(i) Research Operations Office / Finance

- Negotiation of contracts & agreements
- Compensation to participants in case of harm
- Confirmation of indemnity (in conjunction with RGIO)

(ii) Research Governance and Integrity Office

- Sponsor confirmation and organisational risk assessment
- Quality Assurance (audits)
- Investigation of non-compliance