CRASH-19

Aspirin, losartan & simvastatin in hospitalised COVID-19 patients: a multinational randomised open-label factorial trial

SETTING UP THE TRIAL AT YOUR HOSPITAL

Create a strong CRASH-19 team

- All staff responsible for the care of COVID-19 patients should know about the trial: doctors, nurses, administrators, pharmacists
- Provide information to all staff about the trial early – the trial will be most successful if everyone knows about it and feels part of it
- Principal Investigator (PI) has overall responsibility for the trial at site
- PI should identify people to be responsible for trial procedures and spread the workload:
  - Identify eligible patients
  - Obtain informed consent
  - Enter baseline data and randomise participants
  - Prescribe and administer the trial treatment daily
  - Follow up participants and collect outcome data
  - Report adverse events as per the protocol
  - Maintain site file
  - Manage trial drugs receipt and tracking of supplies provided (ideally a pharmacist)
- Each person can be responsible for more than one procedure
- Each person must be knowledgeable and trained to carry out delegated procedures

Trial Training

- CRASH-19 training materials are available
  - On the trial website: https://crash19.lshtm.ac.uk/for-site-staff/training/
  - In the electronic site file (link will be provided by email)
- All staff must complete the training relevant to their role in the trial e.g.:
  - Consent training for those obtaining consent
  - Training on the online data collection and randomisation systems for those responsible for these procedures
- Remote training using videoconference or teleconference can be provided to team members in groups as needed (by LSHTM-CTU or Local Country coordinating team)
- Once relevant training has been completed, staff must log their training on the online form available on the trial website
- Any group training will be logged using a form in your electronic site file
- PI to provide names and contact details of all team members delegated trial responsibilities
- Responsibility for drug prescription can only be delegated to a Clinician

Good Clinical Practice (GCP) Training

- The trial will be conducted in accordance with the International Conference on Harmonisation Guidelines for Good Clinical Research Practice (ICH-GCP), current approved protocol, and relevant regulations.
- The key principles of GCP for trial investigators are:
  - Clinical trials should be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, and that are consistent with GCP and the applicable regulatory requirement(s).
  - The rights, safety, and well-being of the trial subjects are the most important considerations and should prevail over interests of science and society.
  - A trial should be conducted in compliance with the protocol that has received prior institutional review board (IRB)/independent ethics committee (IEC) approval/favourable opinion.
  - The medical care given to, and medical decisions made on behalf of, subjects should always be the responsibility of a qualified physician or, when appropriate, of a qualified dentist.
  - Each individual involved in conducting a trial should be qualified by education, training, and experience to perform his or her respective task(s).
  - Freely given informed consent should be obtained from every subject prior to clinical trial participation.
  - All clinical trial information should be recorded, handled, and stored in a way that allows its accurate reporting, interpretation and verification.
  - The confidentiality of records that could identify subjects should be protected, respecting the privacy and confidentiality rules in accordance with the applicable regulatory requirement(s).
  - Investigational products should be manufactured, handled, and stored in accordance with applicable good manufacturing practice (GMP). They should be used in accordance with the approved protocol.

Good Clinical Practice (GCP) Training

- This trial is being conducted in the pandemic setting where it is critical that every qualified healthcare professional can participate. The trial procedures are similar to those that they perform in their routine clinical work. This will ensure staff without full GCP training will be able to participate

- However, if you would like to complete your GCP training:

  - LSHTM GCP training course available here: https://open.lshtm.ac.uk/enrol/index.php?id=6

  - Nigeria - the CITI training course is required which is available here: https://www.citiprogram.org/default.asp

Trial Drugs and Materials

- Aspirin, losartan and simvastatin will be purchased and provided either by the trial coordinating centre in your country or by your hospital pharmacy. This is to ensure that the quality of drugs used can be assured
- Internet enabled tablet will be provided for use to minimise the need for paper forms
- Electronic methods is being utilised in the trial including:
  - Electronic Investigator Site File (eISF) (Link available via your tablet)
  - Electronic Consent capture
  - Online data collection
  - Online randomisation
  - Online adverse event reporting
- NOTE: Alcohol wipes should be used to clean the tablet and pen before and after use to minimise risk of infection transmission

Electronic Investigator's Site File (eISF)

- Trial Documents available in the eISF include:
  - Protocol, drug data sheets, participant information sheet (PIS) and informed consent forms (ICF), data forms, ethics and regulatory approvals, blank forms and logs
- If paper copies of PIS, ICF and data forms are needed, please print from the eISF. Use online forms as much as possible.
- Sites will need to maintain the following electronic logs:
  - Trial team members log
  - Electronic training logs
  - Randomisation logs
  - Pharmacy drug receipt and use log
- Data forms & associated queries, completed consent forms and completed logs to be saved in the eISF

Communication

- Good, rapid communication between trial team at sites, LSHTM-CTU and any in-country coordinating teams is critical for the success of the trial
- Set up a Team WhatsApp group to establish good communication and teamwork
- Add the CTU WhatsApp number: +44 75 6811 6 668 – this will allow trial related questions to be answered quickly
- Use the group to:
  - share trial information
  - ask questions and advise team members
  - send reminders and updates on the trial
  - advise each other of any recruitment or follow-up needed

Points to think about before starting the trial

- Is everyone informed about the trial?
- Does each shift have a team to conduct the trial procedures?
- How will potentially eligible patients be identified?
- Where will the tablet be kept so everyone can use it to consent, randomise patients and enter baseline and outcome data?
- What process have you agreed to ensure trial drugs are available for use?
- The trial drug(s) need to be given daily. How will staff members know that a patient is in the trial and which arm they are randomised to?
- As patients move to different locations in the hospital, how will you ensure the patient receive the allocated drugs?
- How will you know if a patient is due for discharge or has died?
- How will you track randomised patients to make sure follow-up is done on time?
- How will adverse events be monitored and reported as per the protocol?

Helpful resources available

- See Trial website - https://crash19.lshtm.ac.uk
  - FAQs
  - Training materials
  - Protocol
  - Summary of Product Characteristics for each trial drug
  - Coordinating Centres
    - LSHTM-CTU contact details:
      - All trial related queries: crash19@lshtm.ac.uk
      - Data specific queries: crash19data@lshtm.ac.uk
    - Nigeria Coordinating Centre (NCC) email: Nigeria.crash19@lshtm-ctu.org
    - Pakistan Coordinating Centre (PCC) email: Pakistan.crash19@lshtm-ctu.org

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