TRIAL TREATMENT GUIDANCE

CRASH-19

CRASH-19 will evaluate the effects of **ASPIRIN**, **LOSARTAN**, and **SIMVASTATIN** in patients with suspected or confirmed acute COVID-19 infection compared with **STANDARD CARE**.

Each patient will be randomised to one of the following treatment arms:

- Arm 1: Aspirin 150 mg
- Arm 2: Losartan 100 mg
- Arm 3: Simvastatin 80 mg
- Arm 4: Aspirin 150 mg and Losartan 100 mg
- Arm 5: Aspirin 150 mg and Simvastatin 80 mg
- Arm 6: Losartan 100 mg and Simvastatin 80 mg
- Arm 7: Aspirin 150 mg, Losartan 100 mg and Simvastatin 80 mg
- Arm 8: Standard care control (no additional treatment)

Trial treatment(s) are given in addition to the usual standard of care at the trial hospital.

This is an open-label trial. After entering the Entry Form data on the trial database, the clinician randomising the patient will be given the randomisation number and the treatment to which the patient is allocated. THE RANDOMISING NUMBER MUST BE RECORDED ON THE PATIENT MEDICAL RECORDS BEFORE THE TREATMENT ALLOCATION IS REVEALED

PRESCRIBING

- A Clinician must prescribe the trial treatment(s) – once daily up to discharge or for up to 28 days (whichever is shorter)
- Trial drug(s) must be prescribed on the drug prescription chart (or where all other drugs are prescribed)

DISPENSING

- The trial drugs will be kept securely on the Covid-19 ward or the in the hospital pharmacy and will be dispensed by a pharmacist or delegate
- There is no restriction to brand of aspirin, losartan and simvastatin which can be used. However, they must be purchased from a reliable supplier/manufacturer
- Multiple tablets may need to be taken to achieve required dose e.g. 4 x 20mg Simvastatin

ADMINISTRATION OF TRIAL DRUGS

- Trial drug(s) to be given once daily (until discharge, death or 28 days after randomisation, whichever is shorter) or if the responsible clinician decides to cease treatment for clinical reasons
- Daily dosing should be recorded on the Drug Chart/or equivalent
- If a patient is unable to take oral tablets e.g. patient requires mechanical ventilation after randomisation, drugs can be administered via alternative enteral routes if available (e.g. nasogastric tube or other naso-enteric feeding tubes)
- Ensure that the trial treatment is only administered to the patient to which it is prescribed

***Losartan dose variation*:** If any contraindication develop after randomisation (e.g. hypotension or hyperkalaemia or hypotension) the dose can be reduced to 50mg or stopped. Treatment can be restarted at anytime up to the end of the treatment period when these problems are resolved.

INFORMATION ABOUT THE TRIAL DRUGS

The trial treatments are commonly used drugs. Their summary of product characteristics can be found on the trial website (https://crash19.lshtm.ac.uk/for-site-staff/trial-drug-information/) and in the electronic Investigator's Site File. Appendix 1 of the trial protocol summarises key contraindications to the trial treatments.