SOP TITLE: UK SCREENING, CONSENT AND ENROLMENT PROCEDURES

Purpose

This SOP explains the procedures for pre-screening potential Participants for inclusion in the study and the process for obtaining informed consent, confirming eligibility, enrolment and documentation related to these procedures.

Pre-Screening

Potential UK Participants will be directed to a site-specific web-based eligibility questionnaire for completion.. Site specific lists (Screening and Enrolment Log) of potentially eligible Participants and their contact details will be downloaded from the pre-screening database and securely transferred to sites by the Diabetes Trials Unit (DTU) Team. This will allow the local site team to contact the potential Participants and book a face-to-face appointment for screening/enrolment. These Participants will be identified by a screening number generated by the web-based system.

Consent

As this study enrols healthcare workers or staff working in the healthcare facility, it is important to explain to the Participants that participation in the study is entirely voluntary and it will not have any negative impact on their current employment if they choose to decline to participate.

The informed consent process should be undertaken at the start of the Day 0 visit, before confirming eligibility. If the Participant agrees to take part, a research team member will undertake the informed consent process and obtain consent from the Participant in writing. The Participant can refuse consent to participate even if all the inclusion and exclusion criteria are fulfilled at pre-screening.

Informed consent must be taken prior to confirming eligibility, enrolment and baseline procedures.

Eligibility Assessment

Below are the inclusion and exclusion criteria and some explanatory notes.

Inclusion criteria

These are:

- Participant is willing and able to give informed consent for participation in the study

It will be important to ensure that Participants can stay in the study for up to 5 months.

- Agrees not to self-medicate with chloroquine, hydroxychloroquine or other potential antivirals

We will be using hydroxychloroquine as the active drug so if a Participant takes more chloroquine or hydroxychloroquine, we run the risk of increased toxicity or having an effect on the virus if the Participant is on placebo.

- Adults less than 70 years old at time of consent.

This is the legal age of adults in a given country (>18 in the UK)

- Not previously diagnosed with COVID-19

We must only enrol Participants who have not had a confirmed COVID-19 infection, this includes polymerase chain reaction (PCR) and antibody testing.

- Not currently symptomatic with an ARI (acute respiratory illness)

Participants who have an active ARI cannot be enrolled

- Participant works in a facility where there are cases of either proven or suspected COVID-19

We will be recruiting participants who work in a facility where there are cases of either proven or suspected COVID-19. In the UK this could include doctors, nurses, pharmacists, therapists, hospital porters, dieticians, food service workers, ambulance workers and radiographers, among others.

It is left to the discretion of the site PI to determine who meets this criteria for enrolment.

- Possesses an internet-enabled smartphone (Android or iOS)

Exclusion Criteria

The Participant may not enter the study if ANY of the following apply:

- Hypersensitivity reaction to chloroquine, hydroxychloroquine or 4-aminoquinolines

A known allergy (e.g. anaphylaxis, skin rash) to a drug is a contraindication to its use. This will be determined by history.

- Contraindication to taking chloroquine as prophylaxis e.g. known epileptic, creatinine clearance < 10 ml/min

This will be determined by history. If a Participant had a history of epilepsy in the past or is currently on treatment for epilepsy, he/she will be excluded from the trial.

A creatinine clearance of < 10 ml/min is probably not based on solid science. However, at this low level, a Participant should know if he has renal impairment.

- Already taking chloroquine, hydroxychloroquine or 4-aminoquinolines

This is self-explanatory

- Taking a concomitant medication described below:

This includes the following:

- Antiarrhythmic medications: digoxin, amiodarone, sotalol, flecainide
- Antiparasitic/malarial agents: mefloquine, halofantrine, praziquantel
- Antibiotics: levofloxacin, moxifloxacin, ciprofloxacin, azithromycin, clarithromycin, erythromycin
- Antifungal drugs: fluconazole, ketoconazole, itraconazole, terfenadine
- Psychoactive drugs: lithium, quetiapine, chlorpromazine, thioridazine, ziprasidone, haloperidol, droperidol, methadone
- Migraine treatment: sumatriptan
- Antihistamines: astemizole
- Antiemetics: prochlorperazine, metoclopramide
- Cancer treatments: abiraterone, dabrafenib, dacomitinib, enzalutamide, idelalisib, mitotane
- Other specific drugs: ciclosporin, conivaptan, agalsidase alfa or beta, mifepristone, stiripentol

PIs will also be directed to crediblemeds.org to check other agents that may prolong QT interval

- Known retinal disease

This exclusion criterion is included because long term chloroquine can cause irreversible retinal changes. Although we will only give chloroquine for three months, we do not want to take the risk of exacerbating retinal disease.

- Inability to be followed up for the trial period

Follow -up is important in this study so if a Participant thinks they cannot remain in the study for the required three months (four if they suffer an important drug reaction), they should be excluded.

- Known prolonged QT syndrome (however ECG is not required at baseline)

Chloroquine at the doses we plan to use may cause mild prolongation of the QT interval. If a Participant knows he or she has QT prolongation, they should be excluded.

- Pregnant or trying to become pregnant

Although chloroquine and hydroxychloroquine are generally considered to be safe in pregnancy, pregnancy and breast feeding data are limited therefore pregnant women or women who are trying to conceive are excluded.

- Prior diagnosis of porphyria

Screening electronic Case Report Form (eCRF) and Enrolment

Following informed consent, eligibility will be re-checked and entered in the screening eCRF by a research nurse. Eligibility and the decision to enrol the Participant must be confirmed by the PI or medically qualified designee (per the Responsibilities and Delegation Log) by countersigning the eCRF prior to the IMP being prescribed by the PI or other designated prescriber (may include pharmacist or nurse prescribers depending upon the site requirements).

Once the Participant is enrolled in the study, the Participant ID will be assigned by pharmacy when they assign the study drug kit. The Participant ID is a unique number assigned to the individual Participant and this number will be used throughout the study period on all study documents (e.g. eCRF, sample labels) to replace using the Participant's name.

The screening eCRF must be completed within Axiom Fusion for all Participants who were screened regardless of whether or not they are enrolled in the study (refer to eCRF completion guidelines).

The eCRF will capture the screening date, inclusion and exclusion criteria, confirmation of eligibility, date and time of randomization (if applicable) and Participant ID number (if applicable).

Screening and Enrolment Log

Enter the Participant ID number in the Screening and Enrolment Log received from DTU.

Participant Identification Log

For every Participant enrolled in the study, please complete the Participant Identification Log which includes the following: Participant ID number, initials, complete name, and current address and phone number. The Participant Identification Log is a confidential document and must be kept at the local study site at all-times i.e. never send or share this document with parties other than the site study team.

Once a Participant is enrolled on to the study, baseline procedure will be performed as per protocol. Participants will be randomised to receive either hydroxychloroquine or placebo.

Re-Consent Procedure

Following substantive changes to the trial, participants still actively participating may be required to re-consent. The central trial team will review each substantial amendment and inform sites whether re-consent is required. If required, site staff should contact active participants and on their next scheduled follow-up visit request that if they wish to continue on the trial that they review the new PIS and sign the new ICF.

Related Documentation

- IMP Management SOP
- HCQ Dosing SOP