Guidance for GPs

PRINCIPLE Platform Randomised trial of INterventions against COVID-19 In older peoPLE

PRINCIPLE aims to rapidly evaluate different treatments that could stem the progression of **COVID-19** symptoms, and help ease the burden on hospitals.

Any healthcare professional can facilitate recruitment into PRINCIPLE, by guiding patients through screening, consent, registration, or by performing an eligibility check, or by sign-posting to the trial.

Who do we want to recruit?

Patients with any of the following symptoms, within 14 days since onset:

High temperature | New continuous cough | Change/loss of smell/taste | OR a positive COVID-19 test with any symptoms

AND:

- **Aged ≥65** ***OR***
- **Aged 18-64 and experiencing a shortness of breath as part of COVID-19 illness** ***OR***
- **Aged 18-64 with any of the following known co-morbidities:**
  - Weakened immune system due to a serious illness or medication (e.g. chemotherapy)
  - Heart disease and/or hypertension
  - Asthma or lung disease
  - Diabetes
  - Liver disease
  - Stroke or neurological problem
  - Self-reported obesity or body mass index ≥35 kg/m^2
- Not currently admitted to hospital
- Not previously participated in the PRINCIPLE trial

Exclusion criteria (Colchicine arm)

- Is pregnant or planning on becoming pregnant during the course of the trial
- Is breastfeeding or planning on starting during the course of the trial
- Is a woman of childbearing potential (pre-menopausal female that is anatomically and physiologically capable of becoming pregnant) and not willing to use a highly effective method of contraception
- Is hypersensitive for any of the following: Colchicine, Lactose, Pre-gelatinised Maize Starch, Stearic Acid, Purified Water, Ethanol (96%)
- Has a known blood disorders that require regular hospital appointments
- Severe renal impairment or required dialysis
- Severe liver disease
- Currently taking the following medication: Clarithromycin, Cobicistat, Colchicine, Cyclosporin, Diltiazem, Disulfiram, Erythromycin, HIV protease inhibitors (e.g. ritonavir, atazanavir), Itraconazole, Ketoconazole, Quinidine, Verapamil, Voriconazole
- Inflammatory bowel disease or chronic diarrhoea

Exclusion criteria (Favipiravir arm)

- Aged <50 years old
- Known or suspected pregnancy, or breastfeeding during the course of the trial
- Women of childbearing potential (as described above)
- Known allergy to, or currently taking Favipiravir
- Known history of gout
- Known severe liver disease

University of Oxford | Nuffield Department of Primary Care Health Sciences | Primary Care Clinical Trials Unit | UKRI UK Research and Innovation | NHS

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How to identify the right patient:

- Run a daily search for patients with a recent positive test for SARS-Cov-2.
- Run a search for all patients who might be eligible if they were to become ill. Download the search from **https://sites.google.com/nihr.ac.uk/it-solutions-tv-sm/study-resources/principle**

What to do next:

i) Recruit the patient yourself. Go to https://www.principletrial.org/participants/how-to-join-the-trial and click the '**screening questionnaire'** button.
N.B you are verbally supporting someone to self-consent to the trial and transcribing this information into the online system. Therefore, GCP training is not required. ***OR***

ii) Refer the patient to the study team: **0800 138 0880**, who will guide the patient through enrolment. ***OR***

iii) Refer the patient to **self-enrol**: https://www.principletrial.org/participants/how-to-join-the-trial

2. Check eligibility, either i) **online** using Sentry (sites only) or ii) **over the phone** with the study clinical team or iii) send a patient **medical summary** to the study clinical team to review.
The study team will contact you to request the information required and let you know how to provide it.

3. Patients will be automatically randomised to receive *either* **usual care or a treatment arm (Budesonide or Colchicine if aged 50+, or Colchicine if aged 18-49)**, and the study team will courier a study pack directly to the participant. The study pack contains a participant ID card, self-swab kit, instructions and return envelope, information booklet, and if applicable the medication and medication instruction card.
**If Clinicians wish to prescribe the trial medication themselves, please let the trial team know via email (principle@phc.ox.ac.uk)*. Please see the protocol for medication doses.*

Participant involvement

Participants will start completing their online diary for 28 days and will receive an email reminder with a link to the online diary system. They will be asked daily questions about their symptoms, their medication (if applicable) and contact with healthcare providers (takes approx. 10 mins/day to complete)

- If online access is not possible, the trial team will telephone participants on days 7, 14 and 28 to collect information about how the participant is feeling.
- All participants will be telephoned on Day 3 to check that they have received their participant pack (and medication if applicable) and ask if they have any questions

Please notify the trial team of any Serious Adverse Events (SAEs)

Hospitalisation or death **NOT due to COVID-19,** MUST be reported within 24 hours of becoming aware.

Study Partner

To ensure that patients who may be too unwell at home can still register for the trial, a chosen Study Partner (family member, partner etc.) can help by completing trial procedures and to provide information on the participants' behalf where necessary.

Contact us
Email: principle@phc.ox.ac.uk Tel: 0800 138 0880
Or visit: https://www.principletrial.org

GPs providing information to confirm a patient's eligibility will be reimbursed **£50 per patient**

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