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A clinical trial investigating novel treatments for COVID-19 in the community

Submission date
28/10/2021

Recruitment status
No longer recruiting

Registration date
03/11/2021

Overall study status
Completed

Last Edited
21/03/2025

Condition category
Infections and Infestations

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Despite a high uptake of COVID-19 vaccines, the disease remains prevalent around the world, with many patients experiencing considerable morbidity and requiring hospital admission. The COVID-19 pandemic is having a devastating effect on people's health and society. The risk of complications from COVID-19 is increased in people with underlying health conditions, unvaccinated people, and those in whom the vaccine is less effective, which can lead to significant medical problems, hospitalisation, and death. There is therefore an urgent need to identify treatments for COVID-19 for use in the community early on in the illness that speeds recovery and prevents the need for hospital admission.

Setting up a new clinical trial for each new treatment can be time-consuming and costly. This study is a platform, randomised controlled trial in the community that can test novel agents for treatment of COVID-19 for people at higher risk of complications. Using an efficient, open (no placebo) clinical trial design, we aim to get rapid answers in a flexible and cost-effective manner. The trial will allow further treatments of novel agents, should they become available, whilst the trial is already in progress. We aim to find suitable treatments for widespread use in the community to help those suffering from COVID-19 quicker and prevent Covid-related hospital admissions and death.

Who can participate?
Patients through the UK who have a positive PCR or lateral flow test for COVID-19 which was taken in the last 7 days and are unwell with symptoms of COVID-19 that started in the last 5 days. These symptoms may include, but are not limited to, a high temperature; a new, continuous cough; loss or change to your sense of smell or taste; sore throat; shortness of breath; general feeling of being unwell; muscle pain; diarrhoea; vomiting; fever and cough.

The study website provides more information on how to take part: https://www.panoramictrial.org/

What does the study involve?
Participants will be randomly allocated to receive usual treatment for COVID-19 or usual treatment plus the study treatment. In this study, the study treatment can be changed. Please see the trial website for details of the current study treatment.

What are the possible benefits and risks of participating?
By taking part in this study, participants will be contributing towards the understanding of how doctors can treat COVID-19 and how the symptoms progress. This may help to reduce the duration and severity of symptoms when people fall ill and reduce the burden on the NHS during this crisis. Some participants may be asked to take part in sub-studies which involve providing blood samples and taking swabs. With any medicine, including ones that are already used within the NHS, there is a risk of side effects. Participants will be able to report whether they are experiencing any of these symptoms in the daily diary.

Where is the study run from?
There will be PANORAMIC Hubs across the UK, managed by University of Oxford Primary Care and Vaccines Clinical Trials Unit co-operative (UK). However, all potential participants in the UK can enrol through the trial website.

When is the study starting and how long is it expected to run for?
September 2021 to March 2025

Who is funding the study?
1. Department of Health and Social Care
2. National Institute for Health Research (NIHR) (UK)

Who is the main contact?
Prof. Christopher Butler
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Contact information

Type(s)
Scientific

Contact name
Prof Christopher Butler

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Additional identifiers

Clinical Trials Information System (CTIS)
2021-005748-31

Integrated Research Application System (IRAS)
1004274

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
IRAS 1004274, NIHR135366, CPMS 51313

Study information

Scientific Title
Platform Adaptive trial of Novel antivirals for early treatment of COVID-19 in the community

Acronym
PANORAMIC

Study objectives
The main objective of the trial is to determine the effectiveness of selected antiviral agents in preventing hospitalisation and/ or death in higher-risk patients who are COVID-19 positive.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 19/11/2021, South Central - Berkshire Research Ethics Committee (Bristol REC Centre, Temple Quay House, 2 The Square, Temple Quay, Bristol BS1 6PN, UK; no telephone number provided; berkshire.rec@hra.nhs.uk), ref: 21/SC/0393

Study design
Platform randomized controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
COVID-19 (SARS-Cov-2-infection)

Interventions
A platform trial, in contrast to say a traditional two-arm design, allows multiple arms to be considered simultaneously, and interventions can be dropped and replaced as evidence emerges

for effectiveness or lack of it. The intent is to establish an ongoing trial infrastructure within a master protocol that uses all the data already accumulated for the assessment of current and subsequently introduced interventions. New interventions will only be added after submission to the appropriate approval bodies.

The trial will initially be two arms comparing usual care to usual care + Antiviral agent (name hidden for blinding) treatment. four 200mg tablets (800mg) will be taken by participants every 12 hours (twice a day) for five days. This product is licensed for emergency use in the UK (i.e. under trial circumstances).

Randomisation:
Participants will be randomised using a secure, fully validated and compliant web-based randomisation system. Once deemed eligible, the medically qualified clinician or research nurse from the central clinical team or Hub (as documented on the delegation log) will randomise the participant. Participants will be randomised to one study arm using equal allocation ratios corresponding to the number of eligible arms in the trial. For instance, if there are two active interventions (A & B), the allocation ratio will be 1:1:1 for Usual Care, active A, and active B (respectively), such that 33% of participants are randomised to Usual Care. If there are 3 active interventions, the allocation ratio will be 1:1:1:1, such that 25% of participants are randomised to Usual Care. Patients must be eligible for at least two arms (Usual Care and at least one novel antiviral intervention). Stratification will be by age and vaccination status.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Antiviral agent (name hidden for blinding)

Primary outcome(s)
Non-elective hospitalisations/deaths in higher risk, symptomatic patients with confirmed COVID-19 within 28 days of randomisation measured using patient records.

Key secondary outcome(s))
1. Time to recovery (defined as the first instance that a participant report feeling recovered from the illness) measured using daily online symptom scores. Telephone call or text on days 7, 14 and 28 if data is not obtained through the online diary. Also, at 3 and 6 months.
2. Participant reported illness severity, reported by daily rating of how well participant feels, enabling identification of sustained recovery.
3. Duration of severe symptoms and symptom recurrence measured using GP notes review if available through Oxford RCGP RSC network; otherwise, other sources of routinely collected data after 28 days. Medical notes review for up to 10 years.
4. Contacts with the health services reported by patients and/or captured by reports of patients' medical records up to 12 months
5. New infections in household measured using daily diary for 28 days
6. To investigate the safety of antiviral agents measured by the monitoring of adverse events (AEs as defined in the ISAs) up to 6 months
7. Longer term effects measured using patient contact at three and six months, electronic medical record search for up to one year

8. Cost effectiveness measured using resource use and cost data and EQ-5D-5L at baseline and day 28

Completion date
31/03/2025

Eligibility

Key inclusion criteria
Current participant inclusion criteria as of 02/11/2022:
1. Participant is able and willing to provide informed consent, or their legal representative is willing to provide informed consent
2. Symptoms attributable to COVID-19 started within the past 5 days and ongoing
3. A positive PCR or lateral flow SARS-CoV-2 test*
4. Aged ≥50 years OR aged 18-49 years with one of the following known underlying chronic health conditions considered to make them clinically vulnerable:
4.1. Chronic respiratory disease (including chronic obstructive pulmonary disease (COPD), cystic fibrosis and asthma requiring at least daily use of preventative and/or reliever medication)
4.2. Chronic heart or vascular disease
4.3. Chronic kidney disease
4.4. Chronic liver disease
4.5. Chronic neurological disease (including dementia, stroke, epilepsy)
4.6. Severe and profound learning disability
4.7. Down's syndrome
4.8. Diabetes mellitus (Type or Type II)
4.9. Immunosuppression: primary (e.g., inherited immune disorders resulting from genetic mutations, usually present at birth and diagnosed in childhood) or secondary due to disease or treatment (e.g., sickle cell, HIV, cancer, chemotherapy)
4.10. Solid organ, bone marrow and stem cell transplant recipients
4.11. Morbid obesity (BMI >35)
4.12. Severe mental illness
4.13. Care home resident
4.14. Judged by recruiting medically qualified professional, research nurse, nurse prescriber, prescribing pharmacist, dependent on the ISA for the specific IMP involved, to be clinically vulnerable
*Any positive PCR or lateral flow test taken up to two days before symptom onset and randomisation qualifies.

Previous participant inclusion criteria:
1. Participant or their legal representative is able and willing to provide informed consent
2. Symptoms attributable to COVID-19 started within the past 5 days and ongoing
3. A positive PCR or lateral flow SARS-CoV-2 test within the past 7 days
4. Aged ≥50 years OR aged 18-49 years with any known underlying chronic health condition considered to make them clinically vulnerable:
4.1. chronic respiratory disease (including chronic obstructive pulmonary disease (COPD), cystic fibrosis and asthma requiring at least daily use of preventative and/or reliever medication)
4.2. chronic heart or vascular disease
4.3. chronic kidney disease
4.4. chronic liver disease
4.5. chronic neurological disease (including dementia, stroke, epilepsy)
4.6. severe and profound learning disability

4.7. Down’s syndrome
4.8. diabetes mellitus (Type or Type II)
4.9. immunosuppression due to disease or treatment (e.g., sickle cell, HIV, cancer, chemotherapy)
4.10. solid organ, bone marrow and stem cell transplant recipients
4.11. morbid obesity (BMI >35)
4.12. severe mental illness
4.13. care home resident
4.14. judged by recruiting clinician or research nurse (registered medical practitioner or trained study nurse) to be clinically vulnerable

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
29295

Key exclusion criteria
Current participant exclusion criteria as of 02/11/2022:
1. Patient currently admitted to hospital (inpatient)
2. Previous randomisation in the PANORAMIC trial
3. Currently participating in a clinical trial of a therapeutic agent for acute COVID-19
4. Additional exclusions specific to each intervention arm, if any, as listed in the Intervention Specific Appendices (ISA’s) of currently open trial arms

Previous participant exclusion criteria:
1. Patient currently admitted to hospital
2. Previous randomisation in the PANORAMIC trial
3. Currently participating in a clinical trial of a therapeutic agent for acute COVID-19
4. Participation in an investigational COVID-19 vaccine trial within previous 28 days
5. Additional exclusions specific to each intervention arm, if any, as listed in the Intervention Specific Appendices (ISA’s) of currently open trial arms

Date of first enrolment
08/12/2021

Date of final enrolment
28/03/2024

Locations

Countries of recruitment
United Kingdom

England

Northern Ireland

Scotland

Wales

Study participating centre
Open to all eligible participants throughout the UK
PC-CTU, Dept of Primary Health Care Sciences
University of Oxford
Gibson Building
Radcliffe Observatory Quarter
Woodstock Road
Oxford
United Kingdom
OX2 6GG

Sponsor information

Organisation
University of Oxford

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Government

Funder Name
Department of Health and Social Care

Alternative Name(s)
Department of Health & Social Care, DH

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Funder Name
National Institute for Health Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
Selected, de-identified individual participant data for outcome measures will be available on request, accompanied by a protocol outlining hypotheses and proposed analytic methods, by contacting the corresponding author (panoramic@phc.ox.ac.uk): requests will be considered by a Departmental Committee. A contract should be signed.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	Molnupiravir main results	22/12/2022	28/12/2022	Yes	No
Results article	Molnupiravir virology sub-study results	23/02/2024	26/02/2024	Yes	No
Results article	Molnupiravir cost-effectiveness analysis	25/07/2024	21/03/2025	Yes	No

Results article	Molnupiravir long term results	09/09/2024	21/03/2025	Yes	No
Protocol article		07/08/2023	09/08/2023	Yes	No
HRA research summary			28/06/2023	No	No
Participant information sheet			17/02/2023	No	Yes
Participant information sheet	version 6.0	15/11/2022	21/03/2025	No	Yes
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Protocol file	version 6.0	15/11/2022	22/02/2023	No	No
Protocol file	version 9.0	26/02/2024	21/03/2025	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes