The PANORAMIC Study Summary Sheet

We are inviting you to join this study because we understand you currently have COVID-19.

What you need to know:

- **STUDY AIM:** To find new treatments to help those with COVID-19 to get better quicker and prevent them being hospitalised and even dying.
- Taking part is voluntary.
- People at the highest risk of complications from COVID-19 may be able to get antiviral treatment outside of the trial from the NHS (see: https://www.nhs.uk/conditions/coronavirus-covid-19/treatments-for-coronavirus/). Taking part in the PANORAMIC study will not exclude you from receiving any covid treatments that are available through the NHS.

REQUIREMENTS TO TAKE PART:

- Feeling unwell with symptoms of COVID-19 which have started in the last 5 days.
- A positive test for COVID-19 (SARS-Co-V2) infection. LFT and PCR are both acceptable.
- Aged between 18-49 with an underlying medical condition that can increase chance of having severe COVID-19, ***OR*** aged 50 and over with or without underlying conditions.

WHAT DOES TAKING PART IN THE STUDY MEAN?

- Some people will receive antiviral treatment, in addition to their regular standard NHS care as normal.
- Some people will receive no antiviral treatment within the study but will continue to receive regular standard NHS care as normal.
- The selection is random and is not by any choice.
- You will be contacted by telephone as a minimum on Day 1 (participants of child-bearing potential allocated antiviral treatment only) and Day 2 (all participants). Please see the PIS appendices for full details.
- Participants complete a daily diary for 28 days through the PANORAMIC website; if you are not able to do this for any reason, we will phone you on Day 7, Day 14, and Day 28, to ask about your symptoms and any contacts you may have had with healthcare professionals.
- Virology study: In addition to the main study, some study participants may also be asked to volunteer to provide swabs for viral testing and finger prick blood tests to tell us more about the infection:

- The first 30 participants in each group volunteering for this extra part of the study will have more intensive monitoring and be asked to have daily nasopharyngeal (nose and throat) swabs for 7 days and an additional swab on Day 14. This could be done at a local General Practice set up as a PANORAMIC Hub or be done at home with self-administered swabs. The next 270 participants volunteering for this extra part of the study in each group will be tasked to provide swabs, but less often, and will be asked to return self-administered nasopharyngeal (nose and throat) swabs on Day 1, Day 4, and Day 14. This could be done at local General Practice set up as a PANORAMIC Hub or be done at home. For those participants allocated to antiviral treatment, the first samples will be taken immediately prior to the start of treatment. For those participants allocated to Usual Care, the first samples will be taken the day after they enter the study.
- All participants providing Virology samples will also be asked to take a baseline finger prick dried blood spot sample on Day 1, Day 4, and Day 14. For those participants allocated to antiviral treatment, the first samples will be taken immediately prior to the start of treatment. For those participants allocated to Usual Care, the first samples will be taken the day after they enter the study.
- A telephone call and/or SMS text message/email reminder will be sent to participants enrolling into the Virology study on Day 4, Day 7 (first 30 only) and Day 14.
- Participants volunteering for Virology sampling will be provided with all the materials they need by post.
- Samples which are taken by participants at home must be posted ideally within 24h and posted no later than 3 days after the sample was taken.

SIDE EFFECTS:

- The antiviral treatment has already been taken by people in other studies.
- If you have any side-effects from the antiviral treatment, or if you are admitted to hospital for any reason during the 28-day study period, it's important for you to let us know as soon as possible.

CONFIDENTIALITY and DATA PROTECTION:

- People allowed to look at your health information will be limited to the research team, individuals from University of Oxford, the Sponsor, and the regulatory authorities who check that the study is being carried out correctly. In addition, for us to obtain additional healthcare data about you which is relevant to the study, your date of birth and NHS Number (or equivalent NHS identifier) will be shared with NHS Digital, electronic Data Research and Innovation Service (eDRIS), The Secure Anonymised Information Linkage

(SAIL) Databank or Health and Social Care Northern Ireland (HSC Business Services Organisation/HSC Trusts) (HSC NI) to enable them to securely link, extract and to supply the study team with the data we require. If you are in Scotland and don't provide us with your CHI number during registration for the trial, we may also share your name, date of birth and address to University of Dundee's Health Informatic Centre in order to obtain your CHI number to be able to link with eDRIS. A privacy notice is on the study website for your information: https://www.panoramictrial.org.

For further information on the use of NHS digital and SAIL data within the PANORAMIC study please see the General Notice under the Health Service Control of Patient information Regulation 2002(COPI) (https://www.gov.uk/government/publications/coronavirus-covid-19-notification-of-data-controllers-to-share-information). Following the expiration of the COPI Notice, PANORAMIC will continue to use NHS Digital, eDRIS, SAIL and HSC NI to access and process patient identifiable information without consent under Regulation 5 of the Health Service (Control of Patient Information) Regulations 2002. For more information regarding Regulation 5 please visit: (https://www.hra.nhs.uk/about-us/committees-and-services/confidentiality-advisory-group/guidance-confidentiality-advisory-group-applicants/health-service-control-patient-information-regulations-2002-regulation-5-decision-procedure-research-applications/).

To take part, you will need to:

- Fill in a short form by telephone or on the internet to check that you are eligible;
- Read this information sheet in full;
- Fill in a consent form to agree to take part.

Need more information?

If you would like to speak to a member of the study team, please feel free to get in touch:

Freephone: 08081560017

Email address: panoramic@phc.ox.ac.uk

Platform Adaptive study of NOvel antiviRals for eArly treatMent of COVID-19 In the Community: The PANORAMIC Study

PARTICIPANT INFORMATION LEAFLET

The PANORAMIC Study is trying to find new antiviral treatments for COVID-19 that can be used in the community. We want to test how effective new treatments are at helping people recover sooner and without needing to be admitted to hospital. We are inviting you to join this study because we understand you currently have COVID-19.

This leaflet provides information about the study, including its aims, and tells you about the risks and benefits of taking part.

What is the purpose of the study?

COVID-19

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. In these people, COVID-19 can sometimes lead to significant medical problems, hospitalisation, and death.

Most people with COVID-19 are treated in the community and so we need to find treatments that are suitable for use in the community.

The Study

COVID-19 can cause great suffering, and it stops people from performing their daily activities, affecting their work, education, and caring responsibilities. **The purpose of this clinical study is to find new treatments that help those suffering with COVID-19 at home and in the community get better quicker and without needing to be treated in hospital**. To be able to do this, we aim to test individual possible treatments as soon as they become available.

We are testing new antiviral treatments which might have beneficial effects for the treatment of COVID-19, but which may not yet have a license for use in the UK.

We will also invite some people to provide nasopharyngeal (nose and throat) swabs and finger-prick blood tests so we can find out how the treatments affect the level of the virus in the body, whether there are any other effects on the virus, or any effects on the way your body fights the virus.

All the treatments in the PANORAMIC study have been approved by the UK Medicines and Health Care Products Regulatory Agency (MHRA) for use in the study. The MHRA regulates the use of all medicines in the UK.

People at the highest risk of complications from COVID-19 may be able to get antiviral treatment outside of the trial from the NHS (see: https://www.nhs.uk/conditions/coronavirus-covid-19/treatments-for-coronavirus/). Taking part in the PANORAMIC study will not exclude you from receiving any COVID-19 treatments that are available through the NHS. Please see the relevant section below for further details.

Please see Appendices for specific information about each antiviral treatment.

Can I take part?

To take part, you need to have had a **positive test** for coronavirus (SARS-Co-V2) infection AND you must be unwell with symptoms of COVID-19 illness, which started in the last 5 days. *These symptoms may include, but are not limited to,* a high temperature, a new and continuous cough, loss or change to your sense of smell or taste, a sore throat*, shortness of breath, a general feeling of being unwell, muscle pain, diarrhoea, or vomiting.* Also, to join the study, you need to be either:

Aged ≥50 years

OR

Aged 18-49 with any of the following underlying health condition that makes you more vulnerable to COVID-19:

- Long term lung disease (including chronic obstructive pulmonary disease (COPD), cystic fibrosis and asthma requiring at least daily use of inhalers)
- Long term heart or vascular disease
- Long term kidney disease
- Long term liver disease
- Long term neurological disease (including dementia, stroke, epilepsy)
- Severe and profound learning disability
- Down's syndrome
- Diabetes
- Weakened immune system due to disease or treatment (e.g., sickle cell, HIV, cancer, chemotherapy)
- Having a transplant (e.g., kidney, liver, heart, lung, bone marrow or stem cells)

- Obesity with body mass index (BMI) at or above 35kg/m^2
- Severe mental illness
- Considered by the doctor, nurse, or prescribing pharmacist, as detailed in the PIS appendices, who recruits you to be clinically vulnerable

Do I have to take part?

No, taking part is entirely your choice and voluntary. It is up to you to decide whether to take part in the study or not. A decision to not to take part will not affect the standard of care you receive from the NHS in any way, now or in the future.

In certain circumstances, we are contacting people who may have recently tested positive for COVID-19, and information about this has been provided to the study by NHS Digital in these unique pandemic circumstances. You have the right to opt out of any future communications from PANORAMIC should you wish to do so. PANORAMIC will not keep your data should you choose not to take part. Please see the General Notice under the Health Service Control of Patient Information Regulations 2002 for more information.

(https://www.gov.uk/government/publications/coronavirus-covid-19-notification-of-data-controllers-to-share-information)

We will make a maximum of three attempts to contact you about the study.

What will happen to me if I take part?

If you are interested in taking part, we will ask you to complete a short online form to see if you are eligible. If you do not have internet access or would like to telephone us instead, then you can contact us using the contact details at the end of the document.

Informed Consent

You will be asked to complete a consent form online or by telephone. Instructions on how to fill out the form will be provided, so you will know what to do. You will be able to download and keep a copy of your informed consent form. Before deciding whether or not to take part, you will be able to discuss the risks, benefits, and what you need to do to take part, with a study doctor, research nurse or prescribing pharmacist as detailed in the PIS appendices.

Initial Questionnaire - online

You will then complete some questions online about you and how you are feeling. We will also collect some contact details such as your name, email address, and telephone number. We will also ask you to provide details of a study partner if there is someone suitable for this. This could be a relative, spouse, friend, or carer, if such a person is available, who we will contact for information about you if we are unable to get hold of you for whatever reason. If you are a person of child-bearing potential (i.e., Participants who are physically able to become pregnant regardless of their current contraception methods or relationship status) you will need to agree to taking a urine pregnancy test as part of the screening process. You will only need to take a pregnancy test if you are allocated to an antiviral treatment. A negative pregnancy test result is needed before starting treatment and we will discuss this with you and provide further details if you are allocated to one of these treatments.

If you receive an invalid test result, please contact the study team using the contact details at the bottom of this leaflet to request a replacement a pregnancy test kit as soon as possible. If the delay caused by the need to send a replacement test kit causes you to become ineligible for the study (you are now feeling recovered from your illness), we will need to withdraw you from the study.

Randomisation

After you have registered for the study, your GP, study doctor, research nurse or prescribing pharmacist, as detailed in the PIS appendices, will telephone you to confirm consent and ask you a few questions to check that you are eligible to take part (**Day 0 telephone call**). If you are eligible, during the same telephone call, you will be randomly (like rolling a dice) put into one of the study groups (antiviral treatment with Standard Care or Standard Care) by our computer system. Neither you, your GP, nor the study team can decide which group you will be in, it will be decided purely by chance. If you are allocated to an antiviral treatment, the risk, benefits, and follow-up procedures, will be explained to you at that time.

All participants will receive standard best available care (outside of the study), regardless of whether they are given an antiviral or not. Responsibility for your clinical care remains with the NHS and not the study team. The study team should be contacted about matters relating to the study and NHS services should be contacted about your medical care. If you are randomised to the Usual Care Group, you will receive standard NHS Services available as normal, but we will still

follow you up regardless of which group you are in. This is so we can compare the symptoms and healthcare contacts between those who do and don't receive antiviral treatment. We will inform your GP of which group you have been allocated to.

Study Treatment

If you are randomised to an antiviral treatment group, arrangements will be made for the medication to be delivered to you the following day. You will also receive instructions on how to take it and for how long, and you will be asked to confirm receipt of the medication via text or telephone call. If you are of child-bearing potential (regardless of current contraception methods or relationship status) and you are allocated to an antiviral treatment, your trial pack will also contain pregnancy test with instructions on how to perform the test. If in addition you volunteer to take part in the Virology sampled cohort you will receive a separate Virology sampling kit containing instructions on how to take the samples, sampling materials and any pre-paid packaging by post.

Should your COVID-19 illness worsen at any time during the study, you should not contact the study team about this but contact your GP or other HealthCare services that are open to you i.e., go to the accident and emergency (A&E) department at your local hospital, or contact 111 or 999.

Please see the PIS appendices for further details about the antiviral treatments. You will also be able to call us at any time if you have any concerns about side-effects you think may be caused by the treatment using the study free-phone number: 0808 168 0130. We will contact you to ask if you have experienced any symptoms that could be side-effects of the study treatment. If we are unable to contact you or your study partner, with your consent we may contact your GP directly. We will ask you to return any unused medication in a pre-paid envelope provided if it is decided to stop the treatment before the course is completed.

Follow-Up

After being randomly allocated to a study group, you will receive a text message from us asking you to complete the online questions relating to your symptoms and how well you feel every day for the 28-day study period. If the study team does not receive your daily diary answers online, they will text or telephone you on Day 7, Day 14 and Day 28 of the follow up period and ask you a brief set of questions over the phone.

Day 1 telephone call: If you are of child-bearing potential (regardless of current contraception methods or relationship status) and you are allocated to an antiviral treatment, during this call, we will confirm that you have taken the pregnancy test and obtained a negative pregnancy test result. You will be asked not to take any study medication if the pregnancy test is positive.

Day 2 telephone call:

All Participants, regardless of what group they are allocated to, will receive a call on Day 2 (2 days after randomisation).

If you have been allocated to an antiviral treatment, your GP, study doctor, research nurse or prescribing pharmacist, as detailed in the PIS appendices, will call you the day after you receive your medication to discuss any potential side-effects which you may have experienced since starting the medication, and to answer any questions that you may have.

If you have been allocated to Usual Care Group, you will receive this Day 2 call to confirm you have got your study materials, to answer any questions and to confirm follow up procedures.

Additional telephone calls: If you are randomised to a higher risk antiviral agent you may receive additional telephone calls for safety monitoring purposes. Please see the medication specific appendices for details.

Long-term follow-up: We will also contact you (email, text message, and/or telephone call) at 3 and 6 months after you have started the study to collect information about ongoing symptoms and contacts with healthcare providers. We will collect information from your GP records and data held by central NHS bodies (such as NHS Digital) for long-term follow-up for up to 10 years, to help us better understand the long-term effects of COVID-19 and the study treatments.

Virology sampled cohort: Some study participants may be asked to volunteer to provide nasopharyngeal (nose and throat) swabs and finger prick blood tests: These are research tests, not ones that a doctor or nurse might request, and it will not be possible to provide the results to you. Participating in the virology sampled cohort is voluntary, if you decide not to take part, you will not be excluded from the PANORAMIC study, and this will not affect the medical care you receive during the study. You can indicate your willingness to be approached about this part of the study when completing your informed consent form.

These tests (nasopharyngeal (nose and throat) swabs and finger-pricks) may be done by research staff at a clinic, or by you or a study partner at home, with full instructions and sampling kits provided.

The first 30 participants in each arm will be asked to provide daily nasopharyngeal (nose and throat) swabs at home for a week and an additional sample on Day 14. If you have been allocated to treatment with an antiviral you will need to do your first nasopharyngeal (nose and throat) swab immediately before you start treatment (Day 1). If you have been allocated to Usual Care you will need to do your first nasopharyngeal (nose and throat) swab the day after you enter the study (Day 1). If you are in this initial group, you will receive telephone and/or SMS text and or email reminders to do your samples.

The next 270 participants in each arm will be asked to provide a nasopharyngeal (nose and throat) once on Day 1, once on Day 4 and once on Day 14. If you have been allocated to treatment with an antiviral you will need to do your first nasopharyngeal (nose and throat) swab immediately before you start treatment (Day 1). If you have been allocated to Usual Care you will need to do your first nasopharyngeal (nose and throat) swab the day after you enter the study (Day 1).

All participants volunteering for this Virology sampled cohort will also be asked to do a finger-prick test once on Day 1, once on Day 4 and once on Day 14. If you have been allocated to treatment with an antiviral you will need to do your first finger-prick test immediately before you start treatment (Day 1). If you have been allocated to Usual Care you will need to do your first finger prick test the day after you enter the study (Day1).

We will let you know which group you are in.

Samples you collect at home must be posted back to the study team as soon as possible, ideally within 24h, and within 3 days of you taking the samples. We will provide all the necessary equipment, instructions, and packaging for this with pre-paid postage.

People at highest risk of complications from COVID-19 can get antiviral treatment directly from the NHS

People at the highest risk of complications from COVID-19 may be able to get antiviral treatment outside of the trial directly from the NHS (see: https://www.nhs.uk/conditions/coronavirus-covid-19/treatments-for-coronavirus/). Taking part in the PAN0RAMIC study will not exclude you from receiving any COVID-19 treatments that are available through the NHS.

The following patient cohorts were assessed as potentially eligible for direct access to neutralising Monoclonal Antibodies (nMABs) and antiviral treatments by an independent advisory group commissioned by the Department of Health and Social Care (DHSC)[1]

Cohort	Description
Down's syndrome	All patients with Down's syndrome
Patients with a solid cancer	• Active metastatic cancer and active solid cancers (at any stage) • All patients receiving chemotherapy within the last 3 months • Patients receiving group B or C chemotherapy 3-12 months prior • Patients receiving radiotherapy within the last 6 months

Patients with haematological diseases and stem cell transplant recipients	• Allogeneic haematopoietic stem cell transplant (HSCT) recipients in the last 12 months or active graft vs host disease (GVHD) regardless of time from transplant (including HSCT for non-malignant diseases)
	• Autologous HSCT recipients in the last 12 months (including HSCT for non-malignant diseases)
	• Individuals with haematological malignancies who have
	  ○ received chimeric antigen receptor (CAR)-T cell therapy in the last 24 months, or
	  ○ radiotherapy in the last 6 months
	• Individuals with haematological malignancies receiving systemic anti-cancer treatment (SACT) within the last 12 months except patients with chronic phase chronic myeloid leukaemia (CML) in molecular response or first or second line tyrosine kinase inhibitors (TKI)

[1] For paediatric/adolescent patients (aged 12-17 years inclusive), paediatric multi-disciplinary team (MDT) assessment should be used to determine clinical capacity to benefit from the treatment

	• All patients with myeloma (excluding MGUS) or chronic B-cell lymphoproliferative disorders (e.g., chronic lymphocytic leukaemia, follicular lymphoma) or myelodysplastic syndrome (MDS) who do not fit the criteria above • All patients with sickle cell disease • Individuals with non-malignant haematological disorder (e.g., aplastic anaemia or paroxysmal nocturnal haemoglobinuria) receiving B-cell depleting systemic treatment (e.g., anti-CD20, anti-thymocyte globulin [ATG] and alemtzumab) within the last 12 months

Patients with renal disease	• Renal transplant recipients (including those with failed transplants within the past 12 months), particularly those who:
	  ○ Received B cell depleting therapy within the past 12 months (including alemtuzumab, rituximab [anti-CD20], anti-thymocyte globulin)
	  ○ Have an additional substantial risk factor which would in isolation make them eligible for nMABs or oral antivirals
	  ○ Not been vaccinated prior to transplantation
	• Non-transplant patients who have received a comparable level of immunosuppression
	• Patients with chronic kidney stage (CKD) 4 or 5 (an eGFR less than 30 ml/min/1.73m2) without immunosuppression

Patients with liver disease	• Patients with cirrhosis Child's-Pugh class B and C (decompensated liver disease) • Patients with a liver transplant • Liver patients on immune suppressive therapy (including patients with and without liver cirrhosis) • Patients with cirrhosis Child's-Pugh class A who are not on immune suppressive therapy (compensated liver disease)
Patients with immune-mediated inflammatory disorders (IMID)	• IMID treated with rituximab or other B cell depleting therapy in the last 12 months • IMID with active/unstable disease on corticosteroids, cyclophosphamide, tacrolimus, cyclosporin or mycophenolate. • IMID with stable disease on either corticosteroid, cyclophosphamide, tacrolimus, cyclosporin or mycophenolate. • IMID patients with active/unstable disease including those on biological monotherapy and on combination biologicals with thiopurine or methotrexate

Immune deficiencies	• Common variable immunodeficiency (CVID) • Undefined primary antibody deficiency on immunoglobulin (or eligible for Ig) • Hyper-IgM syndromes • Good's syndrome (thymoma plus B-cell deficiency) • Severe Combined Immunodeficiency (SCID) • Autoimmune polyglandular syndromes/autoimmune polyendocrinopathy, candidiasis, ectodermal dystrophy (APECED syndrome) • Primary immunodeficiency associated with impaired type I interferon signalling • X-linked agammaglobulinaemia (and other primary agammaglobulinaemias) • Any patient with a secondary immunodeficiency receiving, or eligible for, immunoglobulin replacement therapy
HIV/AIDS	• Patients with high levels of immune suppression, have uncontrolled/untreated HIV (high viral load) or present acutely with an AIDS defining diagnosis • On treatment for HIV with CD4 <350 cells/mm3 and stable on HIV treatment or CD4>350 cells/mm3 and additional risk factors (e.g., age, diabetes, obesity, cardiovascular, liver, or renal disease, homeless, those with alcohol-dependence)
Solid organ transplant recipients	All recipients of solid organ transplants not otherwise specified above
Rare neurological conditions	• Multiple sclerosis • Motor neurone disease • Myasthenia gravis • Huntington's disease

Summary of Study Procedures

Day 1 - All participants

- You wil receive a telephone call from a study doctor, research nurse or prescribing pharmacist to: explain risks, benefits, and study processes: confirm your consent;check that you are suitable to take part and if s, you will be randomly allocated to a study treatment.
- After entering the study, you will recieve a link to complete your Day 1-28 daily diary.

Day 1-Participants receiving an antiviral treatment

- If you are of child-bearing potential (regardless of current contraception methods or relationship status) and are allocated to receive treatment with an antiviral, a study team member will call to confirm that you have completed a pregnancy test and that the result is negative before you take any study medication. As soon as you have confirmed that you are not pregnant please start your study medication.

Day 2-All participants

- If you have been allocated to receive antiviral treatment, a study doctor, research nurse or prescribing pharmacist will call you to ask whether you have experienced any side-effects since you started taking the medication.
- If you have been allocated to Usual Care, a member of the study team will call you to check that you have received the study materials, explain about follow-up procedures and answer any questions that you may have about the study.

Days 7, 14 and 28-For participants not completing daily diaries

- If you have been unable to complete your daily diary, you will receive a call from a member of the study team who will ask about your symptoms and whether you have had any contact with health care providers.

Months 3 and 6 after you enter the study

- You will receive a link to complete a questionnaire online about any ongoing symptoms and contact with heathcare providers. We may also call or text you to gather this information.

10 Years after you enter the study

- With your consent, we will collect information from your GP records and data held by central NHS bodies for long-term follow-up for up to 10 years.

Additional tests in the Virology Sampled Cohort

Day 1 - All Participants in the Virology sampled cohort

- Nasopharyngeal (nose and throat) swab *(immediately before starting treatment if allocated to antiviral treatment and the day after trial entry if allocated to Usual Care).*
- Finger prick blood test *(immediately before starting of treatment if allocated to antiviral treatment and the day after trial entry if allocated to Usual Care).*

Days 2-7 - First 30 people in each arm only

- Daily nasopharyngeal (nose and throat) swab.

Day 4 - All participants in the Virology cohort

- Finger prick blood test.
- Nasopharygeal (nose and throat) swab.

Day 14 - All Participants in the Virology sampled cohort

- Finger prick blood test.
- Nasopahryngeal (nose and throat) swab.

What happens if I am admitted to Hospital?

It is important that we know if you are admitted to hospital at any point during the 28 -day follow up period. We need to know about this whether or not you are taking the study medication. We will give you a card that you can carry to let other healthcare professionals know that you are taking part in this study. It is also important that someone close to you knows that you are taking part in the study, so that if you do get admitted to hospital, they can use the details on the card to let us know.

We may also access your medical records and data held about you in central NHS registries and

databases (including NHS Digital, Public Health England, other equivalent bodies, and genetic or other research databases if you have provided samples to them) to collect information on any hospital admission that you may have during the follow up period.

We will send your date of birth and NHS Number (or equivalent NHS identifier) to NHS Digital, eDRIS, SAIL or HSC NI to enable them to supply the study team with additional healthcare data about you, which is relevant to the study. You are free to withdraw your consent for data linkage with NHS Digital, eDRIS, SAIL or HSC NI at any time and it will not affect your ongoing care.

What are the possible disadvantages or side-effects of taking part?

With any medicine, including ones that are already used within the NHS, there is a risk of side-effects. Please see Appendices for details of the side-effects common to each drug. You will be asked to tell us if you are experiencing any of these symptoms in your daily diary, or you can contact the study freephone number. Daily, the study's clinical team will monitor specific, pre-defined potential side-effects that you report in your daily diaries and contact you if required. Please see the medication specific appendices for details about which side-effects will be monitored for each treatment.

If you volunteer to take part in the Virology sampled cohort, we will ask you to provide

Finger prick blood tests and nasopharyngeal (nose and throat) swabs, taking these samples can be uncomfortable but should not cause any serious side-effects. If you are one of the first 30 participants in each arm to volunteer you will be contacted by the study team either by telephone, SMS, or email to remind you to do your tests on the day that they are due.

What are the possible benefits of taking part?

We do not know if the treatments being tested will have additional benefits. Your antiviral treatment may, or may not, help you personally, but we hope this study will help future patients to receive the best evidence based care.

What will happen if I do not want to continue with the study?

If you decide to take part, you can still withdraw at any time without giving a reason. Information collected up to that point will still be used and you or your GP may be contacted if there are

further questions regarding side-effects from study treatments. If you have informed the study team of certain moderate or major side-effects from taking a study medicine not licenced in the UK, the study team would like to contact you and/or your GP until you feel better.

If you wish to withdraw from the study, please contact the study team using the contact details at the end of this document. The decision to withdraw will not affect the standard of care you receive from the NHS in any way, now or in the future. We will ask you to return any unused medication in a pre-paid envelope provided if you withdraw before the treatment course is completed.

Expenses and Payments

You will be reimbursed for your participation through gift vouchers worth a total of £10. You will receive the voucher at the end of your follow up period once we have received your completed symptom diary for the 28-day study period. There will be no prescription charges for study antiviral agents incurred by study participants.

What if there are any problems?

If you have any questions about this study, please contact the Study Team (See the last page for contact details).

The University of Oxford, as Sponsor, has appropriate insurance in place in the unlikely event that you suffer any harm as a direct consequence of your participation in this study.

If you wish to complain about any aspect of the way in which you have been approached or treated, or how your information is handled during the course of this study, you should contact the study team on panoramic@phc.ox.ac.uk or 0808 1560017 or you may contact the University of Oxford Research Governance Ethics and Assurance Team (RGEA) office on 01865 616480, or the head of RGEA, email ctrg@admin.ox.ac.uk.

What will happen to my data?

All information about you and your health will be kept private. The only people allowed to look at the information will be the doctors running the study, the study team and Sponsor, and the regulatory authorities who check that the study is being carried out correctly. A privacy notice is on the study website https://www.panoramictrial.org/.

As part of the study enrolment process we may need to view your general practice and hospital medical records, for example in England, Summary Care Records (SCR) (https://digital.nhs.uk/services/summary-care-records-scr/summary-care-records-scr-information-for-patients) to check your medication, allergies, adverse reactions and 'Additional Information' to make sure that it is safe for you to take study medication. A SCR is an electronic record of important patient information, created from GP medical records. SCR 'Additional Information' includes information recorded in your GP record about your significant illnesses and health problems, operations, and vaccinations you have had in the past, how you would like to be treated (such as where you would prefer to receive care), what support you might need and who should be contacted for more information about you. SCRs can be seen and used by authorised staff in other areas of the health and care system involved in your direct care.

For participants in Scotland, we may access the Emergency Care Summary (ECS), The GP Summary and full hospital medical records (https://static1.squarespace.com/static/601d44b7e8475c7d8be2ea36/t/616ff7032df1493e5488f40a/1634727684605/ecs-faq.pdf).

For participants from Wales, we may access your full GP or Hospital records and information in the Welsh Clinical Portal (https://dhcw.nhs.wales/systems-and-services/secondary-care/welsh-clinical-portal).

For Participants from Northern Ireland, we may access your full GP and hospital records and Northern Ireland Electronic Care Record (NIECR) (https://www.nidirect.gov.uk/articles/northern-ireland-electronic-care-record-niecr) including your Emergency Care Summary Record (https://www.nidirect.gov.uk/articles/emergency-care-summary-record).

We will ask for your consent to view your medical records . Medical records will not be retained by the study team. If your summary care record is unavailable or you do not consent for us to access it, you may still take part in the study as we will obtain this information from your GP.

The analysis of some of the data from the study will be performed by Berry Consultancy with support from statisticians at the University of Oxford. The company is based in the USA, however no information that could identify you will be given to them during this process.

What will happen to my samples?

The nasopharyngeal (nose and throat) swabs provided by participants who volunteer to take part in the Virology Sampled Cohort will be sent to Great Ormond Street Hospital where genetic material will be extracted and used to determine the levels of SARS-CoV-2 virus present and how antiviral treatment affects these levels. These samples will then be transferred to University College London where researchers will sequence the genetic material to see if they can find any variants of SARS-CoV-2 and determine whether treatment with antivirals has any effect on these.

The dried blood spot samples will be sent to the Institute of Immunology and Immunotherapy, Birmingham where researchers will process them to examine the levels of SARS-CoV-2 antibodies and determine whether treatment with an antiviral has any effect on these.

Your anonymised samples, with your consent, will be stored for 12 months following the end of the trial and may be used, with your consent, for future ethically approved research that could take place in the UK or abroad and may involve commercial organisations. If you agree to your samples being used in future research, to meet the traceability requirements of the Human Tissue Act, 2004, your informed consent form will be held until your samples have been used up. If you do not consent to the long-term storage of your samples, they will be destroyed in line with the Human Tissue Act 2004.

What if relevant new information becomes available during the study?

Sometimes during a research project, new information becomes available about the treatment that is studied.

If this happens, the study team will tell you about it and discuss with you whether you want to continue in the study or not.

If you decide to continue you may be asked to sign an updated consent form.

What will happen to the results of the study?

Results will be published in scientific journals, presented at scientific conferences, and

published on the Oxford University departmental website, and may be reported in news media. It will not be possible to identify you in any report, publication, or presentation. If you would like to receive copies of any publications arising from this study, please contact the study team (details are on the last page).

Who is organising and funding the research?

Funding has been provided the by UKRI and National Institute for Health Research. PANORAMIC has been set up by the Primary Care Clinical Studies Unit at the University of Oxford. In-kind contributions: Department of Health and Social Care provided the study medication free of charge to the study.

Who has reviewed the study?

All research in the NHS is looked at by an independent group of people called a Research Ethics Committee (REC). The REC is there to protect your safety, rights, wellbeing, and dignity. This study has been ethically reviewed and was approved by the South Central-Berkshire Research Ethics Committee (REC Reference:21/SC/0393).

This study has also received approval from the Medicines and Healthcare products Regulatory Agency (MHRA).

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