PANORAMIC (COVID-19 Antiviral Platform)

Frequently Asked Questions

V1.0, 16 December 2021

My enquiry relates to...

CONTACT INFORMATION AND ROUTES	
Which contact details for the team at Oxford should we use?	Email: panoramic@phc.ox.ac.uk Telephone: 0808 156 0017 The number goes direct to the trial team staffed Monday-Friday 8.30 – 17.30. There is a voicemail service for out of office hours. Any urgent calls from participants and clinicians outside of these times can be directed to the 24-hour safety line.
Will there be a helpline for participants and healthcare providers, and will it be available over the weekend?	Yes, there is a 0800-number listed on the trial documentation. This will come directly to the central trial team. This safety line will be manned 24 hours.
STUDY DELIVERY	
How can sites identify potential participants?	By searching for positive COVID-19 cases in GP records. EMIS and SystmOne searches will also be provided to study teams, and an NHS Digital platform will be made available to support this activity.
Can patients and sites take part in both the 'PANORAMIC' and 'PRINCIPLE' trials?	These are synergistic trials, with running both of them at sites an option (they are compatible, from a site perspective, and will work together). However, patients can only take part in one trial of an acute COVID therapeutic at a time (even if randomised to usual care in one of the trials) and should be considered for recruitment into 'PANORAMIC' first. If they are ineligible for 'PANORAMIC' or would prefer to take part in 'PRINCIPLE', they can then be offered involvement in 'PRINCIPLE', but patients can't take part in both trials.
Will sites / Hubs be required to take part in the sub-studies, or can they only take part in the initial study?	It is hoped that all sites / Hubs will be able to take part in the sub-studies, as tasks for the sub-studies will be kept to a minimum. However, sites that can't take part will not be disadvantaged and will be able to take part in the initial study only.

<table>
<tr><td>Who can make the calls required on Day 1 and Day 2?

Will the central study team be able to support with Day 1 and Day 2 calls during weekends?</td><td>The Day 1 call can be made by anyone, as this is not a safety call. The Day 2 call should be made by a medically qualified clinician or research nurse (GCP trained) to allow for decision making in response to the safety call. Local NIHR CRN teams can support with these calls. Please see the table below.

When NIHR CRN staff are completing these calls, if any SAEs are identified, it will be the responsibility of the Hub PI to complete the form. Alternatively, the central study team can be alerted to the SAE and complete the online SAE form.

It is preferable that Hub sites or local NIHR CRN support perform the Day 1 and Day 2 calls on weekends. The central study team will be discussing this with practices as part of the feasibility to ensure that all activities are covered.</td></tr>
<tr><td colspan="2"><table>
<tr><th></th><th>Day 0</th><th>Day 1</th><th>Day 2</th></tr>
<tr><td></td><td>Informed Consent, Eligibility, and Randomisation</td><td>Safety Call (For Women of Childbearing Potential ONLY)</td><td>Safety Call</td></tr>
<tr><td>IMP Arm</td><td rowspan="2">Clinician/Research Nurse (from hub)</td><td>Can be made by clinical or non-clinical staff at the hub.</td><td>Clinician/Research Nurse (from hub)</td></tr>
<tr><td>Usual Care</td><td>N/A</td><td>Can be made by clinical or non-clinical staff at the hub.</td></tr>
</table></td></tr>
<tr><td>If the IMP has not arrived by the time of the Day 2 safety call, what should site teams do?</td><td>If the IMP has not arrived within five days of the participant experiencing COVID-19 symptoms, the participant should be withdrawn and told to return the IMP.</td></tr>
<tr><td>Who will be responsible for making the follow-up calls?</td><td>The central study team will make the follow-up calls at 3- and 6-months post randomisation, and on Days 7, 14 and 28 if no daily diary data has been returned from participants.</td></tr>
<tr><td>How will 'PANORAMIC' run alongside the nMAB clinical pathway?</td><td>The intention is for PANORAMIC and the nMAB pathway to run alongside one another, to ensure the greatest possible coverage of treatments and prophylaxes for the wider population.

Those eligible for the nMABs (very seriously impaired immunity, extremely vulnerable) are a much smaller group than those eligible for 'PANORAMIC', which, for example, includes everyone aged over 50.

NHS Digital is working to screen out patients eligible for nMABs from the 'PANORAMIC' specific feeds of potential participants. Please see the Government website for further information.</td></tr>
</table>

For patients randomised to the intervention arm, do the Hub sites take on clinical responsibility of the referred patient in terms of managing COVID-19 symptoms for 28 days, or just for the 5 days whilst the patient is taking the IMP?	The clinical responsibility for all patients in the study should remain with their registered GP. The trial takes responsibility for adverse events of medication but does not provide any responsibility for clinical care. So, if a patient came from a Spoke and was in the trial, they would remain under the care of that practice. This would apply also to usual care patients, where usual care is determined by the responsible clinician in the practice or in the hospital, not by the study team or the protocol. As Spokes retain clinical responsibility for their patients, we would ask that Hubs liaise with Spokes to gather required data if AEs or SAEs are reported.
Who is responsible for the reporting and monitoring of adverse events?	Participants will complete their diary daily, which includes questions on potential adverse events. Anything that constitutes a potential adverse event will be alerted to the trial team automatically. However, if the Hub clinician becomes aware of a safety event, this must be reported to the trial team in the usual way to ensure compliance with safety reporting processes. The Hub site will need to work with their Spokes to raise awareness of this.
How will diary completion and pregnancy tests be managed for incapacitated adults?	This should be conducted as per procedures for any other incapacitated adult taking part in a research study, and support should be offered by the participant's usual caregiver.
If a positive lateral flow test is used for study entry, how does the site / Hub inform the study team of the PCR result following enrolment?	We will ask the participant to confirm their result, however, we may gather this data through follow up mechanisms later in the trial; therefore, the trial team will be in touch to confirm any outstanding results.
Unwilling to use contraception (for both men and women) or confirm a negative pregnancy test (for women) is an exclusion. The patient will receive the medication pack (including pregnancy test); what stops the patient from taking the IMP anyway?	All individuals of childbearing potential must agree to use an effective form of contraception while receiving the trial IMP. For every participant randomised into the trial, there will be a two-way conversation between the participant and a member of the clinical team prior to randomisation. The requirement for a pregnancy test for women of childbearing potential prior to treatment will be emphasised during this call, as well as in the patient facing materials. Participants will also need to consent to taking a pregnancy test as a condition of participating in the trial. The MHRA approved this approach and the potential risks associated with sending the pregnancy test with the medication, in order

	to successfully and safely recruit participants into the trial within the 5-day symptom window. There is no need to be concerned about contraception after the 28-day period outlined in the protocol. 28 days is a highly conservative margin in that the drug should be eliminated within 5 days after the course of molnupiravir has been completed.
What electronic systems will be used for data collection including the electronic diary?	The electronic system being used is Spinnaker. In addition to collecting data and electronic diary completion, Spinnaker is able to collect screen failure data at a Hub level.
Will Hub site PIs need to call participants recruited via the Hub if this is deemed clinically necessary, or will this function be performed by the central study team?	Usual clinical care remains the responsibility of the participants' usual clinician. Any safety issues are followed up by the central study team.
Will Hubs be expected to monitor drug compliance remotely for participants recruited via the Hub, or will this be done by the central study team?	No, this data is collected through the daily diary.
Can patients without smartphones / computers / internet access be able to take part in the trial, and how do they provide their daily diary updates?	Yes, the central study team will telephone participants with no internet access to conduct the follow-up calls and daily diary updates.
What is the format of the training for the study likely to be, and when will this be set up and delivered? Is the training going out to both Hubs and Spokes?	The training is pre-recorded and links to the training are currently being sent to all Hub sites as confirmation of their involvement is finalised.
Who will be required to complete the delegation logs for the study?	Hub staff and NIHR CRN staff; we will ask NIHR CRN staff to sign the central delegation log and will provide them with all training materials. If NIHR CRN staff are supporting Hubs, they will need to be signed onto the Hub delegation log. There is no training or delegation log required for the Spoke sites.

Will there be a requirement for face-to-face visits as part of the study?	There is no requirement for face-to-face visits for the molnupiravir arm of the study. There may be face to face visits as the trial progresses with new arms.
Are long-term follow up visits to be conducted by the Hub sites?	Follow up activities are anticipated to be via an online survey. Hubs will only become involved if additional patient information is needed.
SITE IDENTIFICATION	
Can secondary care sites take part in the study?	Any NHS facility that is capable of doing the tasks required can be a site, including secondary care and community Trusts.
Would a single whole- region Hub be considered if all recruitment can happen remotely?	Yes, if follow-up can be conducted for all participants and we can organise the safe delivery of the IMP to participants randomised to receive it. Single GP practices (without associated Spokes) may also be Hub sites for this study.
Can community pharmacies be a full Spoke in a Hub and Spoke arrangement?	It is not expected that community pharmacies will have access to the levels of information required to identify and contact participants, and so it is not thought that community pharmacies will be able to operate as full Spoke sites.
Do GP practices have to join the RCGP RSC to take part in the trial?	Not necessary; 'PANORAMIC' is not formally linked with the RSC and does not rely on RSC data.
Can sites come on board at a later date after the study has opened?	Additional sites can come on board as soon as possible after the study has opened at the first tranche of Hub sites.
Do new Spokes for existing Hubs need to complete an expression of interest?	No, Spokes are to be managed by the Hubs, so no further information is required by the central trial team.
What information will Spoke practices receive and when?	There are no trial information packs for Spokes. The communication and arrangements with Spokes are at the discretion of the Hubs.
Will standard agreements be used (OID, etc.)?	The Primary Care CTU (central study team) will provide a site agreement.

Is there an average patient list size that you are looking for Hub and Spoke models?	There is no standard list size requested by the central study team.
When and how will the virology sub-study sites be determined?	Sites will be invited by the central study team to take part, depending on proximity to a clinician facility delivering the sub-study.
PROTOCOL	
As this is an adaptive study, what is the process that you are following to inform staff and sites when new arms are added to the study?	We will inform all sites / Hubs in a timely way to any changes in the protocol, including the addition of new arms and the suspension of existing arms. New versions of the protocol will be circulated. Any urgent updates will be communicated to all sites / Hubs / contacts directly from the central study team.
At what stage of symptomatic disease should participants be contacted and recruited?	As early as possible. We aim to get the study medication to the participant within 24 hours after randomisation. The goal is to have people start the antiviral agents within 5 days of symptom onset.
The current IMP does not need any special storage and can easily be held on site. **Will future arms also be suitable for storage at Practices, or will special requirements be managed by the central study team?**	There are no specific storage requirements for the first IMP included in the study. As further IMPs are included this may change. Please refer to the IB/SmPC for each IMP for further details. Arrangements will be made for future IMPs when they have been identified.
CONSENT / ELIGIBILITY	
Who can screen patients, confirm eligibility and consent?	Only a medically qualified clinician or research nurse (GCP trained) can undertake the eligibility assessment and consent patients. This does not currently include clinical pharmacists, paramedics, physician associates, advanced clinical practitioners, or specialist mental health nurses, however this will be explored further with the MHRA.
Who can undertake pre-screening activities?	Any practice staff member can approach patients and undertake pre-screening activities. However, any interested

	patient will need to be referred onto a medically qualified clinician or research nurse to confirm eligibility and take consent.
How can consent be taken?	Either face-to-face, by telephone or via a virtual call.
What is the central study team's role in consenting patients?	The central study team will screen and consent patients who present centrally through the trial website. This is an additional route into the study which will run alongside the work of the sites / Hubs. Patients who sign up to take part through this route will be managed centrally.
When making a clinical referral from a Spoke site to a Hub site, is there a requirement that the Spoke assesses a patient's eligibility?	Spokes can refer patients they believe to be potentially eligible onto Hubs. Full eligibility will be confirmed at the Hub.
Can NIHR CRN teams consent patients for practices?	Qualified NIHR CRN staff will be able to consent patients where this is required, such as where patients or Hubs are in remote locations.
Can single practices take part in consenting even if they are not part of a Hub or Spoke?	No.
Is there anything to prevent participants recruited through a Hub, and allocated to usual care, attempting to be re-consented through the central study team?	There are processes in place to ensure that participants cannot access the trial more than once.
Are PCR tests required for patients to be eligible for this study?	A positive lateral flow test in a person who has symptoms of COVID-19 is sufficient for randomisation purposes, but they also need a positive PCR test result to be included in the main analysis, so they should be asked to get a PCR test to confirm the lateral flow test result. If this confirmatory PCR test is negative, the participant may continue in the trial, but the results will be analysed separately.
How will recruiting sites be made aware of positive lateral flow tests?	This will come through the web interface that is being developed.
Will LAMP testing be considered in the same way as a positive lateral	There are different LAMP tests: the RNA RT-LAMP test on a swab has a sensitivity of 95% and specificity of 99% in the

flow test?	case of a person with symptoms. This should apply in the same way as a positive lateral flow test; however, the participant should also get a PCR test to confirm.
Can A&E signpost patients to this study?	Yes, A&E departments where patients present, but are not ill enough to be admitted, can signpost patients to this study. In addition, any GP practice (whether involved in the study or not), NHS 111, and NHS Test and Trace can signpost to the study website.
Can A&E consent COVID-19 positive patients who are not hospitalised, for the patient to be followed up by the central study team?	Consent can only be taken by those who have been delegated the task, are appropriately trained, and are linked to a site. We also need someone at that site to conduct the eligibility assessment and randomisation.
Can patients admitted into a mental health hospital for a relevant condition take part in the trial?	Patients admitted to a long stay facility, rather than for acute care of COVID-19, are potentially eligible. Patients whose normal place of residence is a healthcare facility, such as a long stay psychiatric unit, are not eligible.
How is the start of the 5-day (120 hours) window defined?	From symptom onset. A positive PCR test any time within the week prior to randomisation is required. A lateral flow test in the context of symptoms attributable to COVID-19 is acceptable for eligibility purposes, but the participant needs to have a PCR test to confirm before they can be included in the main analysis of the trial.
What is the definition of severe mental illness, in terms of participants who are eligible to take part in the trial ages 18-49?	For severe mental illness, the evidence suggest that the following should be included: ○ Bipolar affective disorder ○ Psychosis ○ Schizophrenia or schizoaffective disorder ○ Severe depression
Are vaccinated patients and those who have had COVID-19 previously eligible?	Yes, patients who have received a vaccine (either deployed or through a vaccine study), as well as participants who have previously had COVID-19 are eligible. This is in addition to patients for whom this is the first confirmed COVID-19 infection.

If a participant who is registered with a Hub GP practice self-refers through the central team, how can the Hub site visualise this?	When a participant self-registers through the PANORAMIC website and they list their practice as a known Hub, that registration gets diverted to the Hub's part of the Spinnaker database for them to go on and complete randomisation. There is no email alert for this, however all Hubs have been shown where to find the registration list and these participants are listed on their homepage when they log in.
CONTRACTING	
Will PIC mCTA agreements need to be in place between Hub sites and Spoke sites?	Spokes will not be acting as true PIC sites; they will be doing a clinical referral to the Hub for treatment options. However, a category C contract will be required between the Host or Network to secure / transfer funding (to pay the service support costs).
The site agreement suggests that the GP practice or PCN would indemnify Oxford University; please could you clarify?	This is the standard wording from Oxford University and is included in the case of the site not following data protection laws.
Are Letters of Access required for CRN staff or staff from other sites to support the study in primary care hubs?	No.
RECRUITMENT AND RANDOMISATION	
Do Hubs sites undertake their own randomisation?	Hub sites will complete randomisation for participants they are consenting.
If a patient signs up through the central study portal, is there a process to take them off the list at the GP practice so they are not being contacted twice?	This is something we are working on at the moment. We are aiming to exclude duplication in the feeds to the Hub sites and the central study team. Once a participant has been approached and a decision is made about eligibility and participation, an 'Actioned' tab is available which will mean that person is not repeatedly contacted.

How should Hub sites deal with people who decline to participate as this is a clinical referral? Will an email back to the Spoke site suffice?	This is at the discretion of the Hub site.
The protocol mentions patients will be receiving a £10 voucher. Who will send them to the patient?	The central study team will send these out to all participants at the relevant time.
Can Hub sites randomise on Sundays and on national holidays?	Sites are given information regarding cut off times for randomisations when they are opened. Currently randomisations cannot occur on a Sunday. Sites need to make their own arrangements to cover any calls that are necessary for their patients on national holidays or Sundays.
DOCUMENTS	
Will central resources be provided, e.g., scripts to be followed when contacting patients and safety follow up calls?	Central resources will be provided. Consent and screening calls are led by the CRFs within the database; there are no additional scripts. Work instructions for Day 1 and Day 2 calls have been made available for activated sites.
Is there a plan to make patient information available in different languages?	Not at this time, but videos explaining the trial to potential participants will be made available in 11 languages.
Is there a template text message Spoke sites can use to contact patients?	There is not an official template for Spoke sites, but they can use the same template recruiting GP Practices have been given, which can be found on the study website in the 'Text Message Template' document. If desired, the PIS may also be embedded in the text message.
IMP SOURCING AND PHARMACY CONSIDERATIONS	
What is the storage requirement for the IMP at sites, and does it need to be temperature monitored?	All study medication is to be kept in a dry area, stored at 1° to 30°C (59° to 86°F). We will ask participants to store the medication at room temperature. The IMP does not need to be temperature monitored.

Will Hub sites be receiving the IMP on site, or will this be sent out centrally by the trial team?	Initially this will be sent centrally. When we are ready to supply the IMP to sites, we will be in touch. If sites are unable to support the storage and dispatch of the IMP, there will be an option for Oxford to support this in the long term. Individual arrangements will be made with Hubs when the option for IMP dispatch from the Hubs is available.
Will all Hub sites be expected to store and dispatch the IMP, and will a pharmacist be required at the Hub site to dispense it?	Ideally all Hub sites should store and dispatch the IMP as this allows rapid access to the drug for participants. A pharmacist isn't necessarily required at the site; a GP or their delegate can dispense the IMP.
If a patient has a positive pregnancy test result, how do they return the study medication?	We are providing patients with special delivery envelopes to send the study medications back to the trial team.
Are Advanced Nurse Practitioners able to prescribe the IMP?	There are no prescriptions for the trial. The IMP is dispensed as part of the trial by the consenting / randomising clinician.
How can COVID-19 positive participants collect the study medication, can medication be couriered to participants?	This can be picked up from the practice by a non-infected friend or relative, or local courier services; both are viable options.
Is the NHS volunteer service an option for delivering the study medication to local participants?	There is nothing formal in place with the NHS volunteer scheme for 'PANORAMIC', but this can be actioned locally.
COMMUNICATIONS	
What is the study website URL?	https://www.panoramictrial.org/
Is there a comms team to handle press interest in this study?	Yes, there is a team at the CTU dealing with communications.
Has there been national engagement with PCR test sites, and are there leaflets about the study that can be handed out at test centres?	All NHS facilities including testing centres, NHS walk-in / drive-through centres will be able to inform potentially eligible participants about the trial and refer them to the trial website and / or trial team.

Will there be videos for patients to understand how to self-test?	Participants are not required to self-test as part of the trial yet. Once the virology sub-study is up and running, these will be available.
OTHER	
Can molnupiravir be accessed outside of the trial?	Certain patients may be able to access the drug outside of the trial, but GPs won't be able to prescribe it that way. There is a highly vulnerable group of people that may be able to access the drug if they are not suitable for nMAB infusions, but that population will be handled and cared for in hospitals. The question of 'PANORAMIC' is therefore about primary care access to the drug in at risk groups, but not the highly vulnerable group.
We have received comms that say the drug can be accessed outside the trial – is this correct?	The very high-risk patients may receive the IMP in secondary care if infected but are more likely to get nMABs. Please see the Government website for further information.
Why is there a need for a trial when the drug is licenced and has been shown to be effective?	The data has come from an unvaccinated population. Every medication has potential downsides, as well as potential lifesaving benefits in this case, but we don't know what this drug will do in a vaccinated population and what it will do for potential resistance to the virus. We will soon be launching the virology sub-study, and we don't know cost-effectiveness. Further, the licence the drug has received is conditional marketing authorisation, so requires equipoise.
Will a Smartcard be required to access the NHS Digital platform?	Yes, a smartcard will be required to access the platform.
Will this study be part of the NIHR Associate Principal Investigator scheme?	Yes.
Are you able to share a statement from the HRA that states that the use of clinical referral pathways is approved?	PANORAMIC will utilise a Hub and Spoke approach to the identification (at Spokes) of patients, potentially eligible to receive the novel intervention, and their referral to Hubs.

	The primary purpose of this referral is not inclusion of an individual within a research study but to offer a patient an intervention that the referring clinician believes may be in the best interest of that patient. The primary purpose is care. That care is being delivered in the context of a real-world trial, as directed by the Secretary of State, but the purpose of the referral is care, not research.