PAxlovid loNg cOvid-19 pRevention triAl with recruitMent In the Community in Norway

Short title: PANORAMIC Norway
Ethics Ref: 578741

EudraCT Number: 2022-003244-27

Study phase: 3

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Date and Version No Norwegian protocol: 23rd March 2023 Version 2.3

This Clinical Study Protocol has been reviewed and approved by the Sponsor in order to ensure compliance with Good Clinical Practice. This Clinical Study Protocol has been reviewed and approved by the Principle investigator in order to ensure compliance with Good Clinical Practice.

Signature of Sponsor representative

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Protocol Summary

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Background: Despite high uptake of vaccination against COVID-19, the disease remains prevalent in Norway and in many countries around the world, with many patients continuing to experience considerable morbidity and requiring hospital treatment. 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. A considerable burden of long term complications has been reported after COVID (named long COVID) even after home isolation of mild cases, but are particularly associated with more severe disease, and an early therapeutic intervention could potentially also prevent this COVID-19 related morbidity.

Aims and objectives: The study hypothesis is that antiviral treatment for acute Covid can prevent occurrence of persisting symptoms at 3 months and beyond. The primary objective is to assess whether a 5-day course of nirmatrelvir/ritonavir (Paxlovid ®) treatment for patients with acute Covid verified by positive SARS-CoV-2 PCR test result or positive lateral flow test, can reduce the prevalence of persistent symptoms at 3 months compared to placebo. The overall aim of the research is to identify a tool to prevent long COVID, and reduce its burden on society.

Interventions: This is a randomized clinical trial assessing whether healthy adults (P) treated with Paxlovid (I) for acute Covid versus those treated with placebo (C) will have reduced probability of suffering persistent symptoms at 3 months and beyond (O). Participants will be randomized 1:1 to two arms of the trial. Participants in the intervention arm will receive a standard 5-day treatment course Paxlovid (nirmatrelvir plus ritonavir) in addition to standard of care. Participants in the control arm will receive a 5-day course of placebo tablets, with the same appearance and quantity, in addition to standard of care. Participants will be randomised to receive either the antiviral agent Paxlovid (nirmatrelvir plus ritonavir) in addition to standard of care or Placebo plus standard of care.

Eligibility: Participants who meet the following inclusion criteria may be eligible to take part in the trial:

- Symptoms attributable to COVID-19 starting within the past 5 days and ongoing
- A positive PCR SARS-CoV-2 test or a positive lateral flow test. Any positive PCR test or a lateral flow test taken between two days before symptom onset and randomisation qualifies
- Age ≥ 18 years and <65 years
- Participant is able and willing to provide informed consent, and able to comply with all study visits
- Patient not currently admitted to hospital
- No comorbidity which constitutes an indication for active antiviral treatment with Paxlovid as judged by the investigator
- No chronic renal impairment
- No chronic liver disease or liver impairment
- No previous randomisation in the PANORAMIC Norway trial
- Not currently participating in a clinical trial of a therapeutic agent

- Not currently taking Paxlovid
- No known allergy to Paxlovid
- No use of concomitant medication contraindicated for the treatment of Paxlovid*
- Not currently pregnant or lactating
- Willingness to take a pregnancy test prior to starting study treatment (Participants of childbearing potential)
- Willingness to use highly effective contraceptive until 7 days after completing Paxlovid (Participants of childbearing potential or have a partner of childbearing potential)

Outcomes: The primary endpoint will be presence of pre-defined symptoms of long COVID at 3 months from randomisation). The secondary outcome will be all-cause, non-elective hospitalisation or death within 28 days of randomisation. Secondary outcomes will further include time to self-reported recovery; participant reported illness severity; duration of symptoms and symptom recurrence; healthcare service use; participant reported household infection rate; safety outcomes and cost-effectiveness outcomes; symptoms and well-being at six months (with determination of proportion with Long Covid) from randomisation. See Table 1 for details of objectives and outcome measures.

Study design: This is a two-arm 1:1 randomized double-blinded placebo-controlled clinical trial. The study is designed to assess whether healthy adults (P) treated with Paxlovid (I) for acute Covid versus those treated with placebo (C) will have reduced probability of suffering persistent symptoms at 3 months and beyond (O). An external statistician will produce a randomization list prior to the start of the trial. At the time of inclusion in the study, study personnel will blindly allocate participants to receive active ingredient or placebo according to the randomization list. All enrolment (screening, eligibility review, informed consent and baseline data) will be conducted by the trial team, with follow-up procedures (electronic diary) conducted remotely with participants or their chosen support person (Study Partner) using the trial website or a telephone call with the trial team. Any hospitalisations and deaths will be recorded.

Recruitment: A central trial team will recruit and allocate participants to the next medication/Placebo number. A participant pack containing Paxlovid or Placebo will be given to the participant or their Study Partner, which is a person appointed by the participant to act on their behalf, for instance to collect study medication at the central study site. During the study period, further recruitment sites and PraksisNett collaboration will be considered.

Data to be recorded: Demographic features including age, gender, comorbidity, allergies, medication history and present medication, COVID vaccine history and previous COVID-19 will be captured at baseline. In the online diary (completed each day for 7 days, weekly for 28 days, and at 3 and 6 months) and during telephone calls, participants or their Study Partners will rate the severity of symptoms including how well they are feeling, record contacts with the health services (including hospital admission), record study medication use, resource use, sick leave, and new infections in the household. Follow-up beyond 28 days after randomisation will be by accessing medical registries and by participant questionnaire for information relevant to the longer-term consequences of COVID-19 at three and six months from randomisation. To investigate the impact of trial interventions on the longer-term effects of COVID-19, we will also remotely follow-up participants, for up to 1 year.

Exploratory subprojects: 1. A subgroup of up to 500 patients will be asked to attend a face-to-face visit or to donate a microbiological or blood sample for the purpose of the study, at 3, 6 and 12 months after inclusion. 2. A smaller group of 100 patients, with and without symptoms at 3 months will be included in a study on brain damage, including neurocognitive, EEG and MRI investigations.

Numbers to be randomised: An estimated maximum of approximately 1000 participants per arm will be required to provide approximately 90% power for detecting a 20% relative reduction in long COVID symptoms in an experimental arm relative to Placebo, based on the assumption of an underlying 30% prevalence of long COVID at 3 months in the placebo arm, and an intervention lowering the long COVID rate to 22%.

Estimated study timelines for data collection:

Start of study: 01-Apr-2023
First patient in (FPI): 01-Apr-2023
Last patient in (LPI): 01-Aug-2024
Last patient out (LPO): 01-Aug-2025

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1. BACKGROUND and RATIONALE

Despite high uptake of vaccination against COVID-19, the disease remains prevalent in Norway and in many countries around the world, with many people continuing to be infected and requiring hospital admission. COVID-19 causes considerable suffering, including loss of ability to perform activities of daily living, loss of educational and work opportunities, and inability to perform caring duties, with far reaching personal and societal consequences[1,2]. A considerable burden of long term complications has been reported after COVID (named long COVID) affecting more than 50% of cases after home isolation of mild cases, but are particularly associated with more severe disease where up to 80% have symptoms after six months (2). Nearly half of home isolated individuals still had persisting symptoms 12 months after COVID-19, with high risk of fatigue, memory problems, concentration problems and dyspnea[3]. Worryingly, the prevalence of memory problems increased overall from 6 to 18 months. Reports have shown some reduction of persisting symptoms when patients have been vaccinated before SARS-CoV-2 infection, but the degree of protection is yet to be established[1]. People with underlying health conditions, unvaccinated people, and those in whom the vaccine is not effective are at increased risk of more severe disease[4]. Moreover, new 'vaccine escaping' variants may yet emerge, potentially expanding the population at risk of persisting and/or relapsing symptoms of COVID-19. Early treatment with antiviral agents may prevent progression to the later phase of COVID-19. Therefore, there is an urgent need to identify treatments for COVID-19 for use in the community early on in the illness that prevent the need for hospital admission, improves time to recovery and potentially reduce long term sequelae[5, 6]. Antiviral agents may reduce viral load and shedding, and use of antiviral agents may lead to the emergence of resistance to novel antiviral agents, but the impact of novel antiviral agents on shedding and resistance is not yet known[7]. In a placebo controlled trial, treatment of symptomatic Covid-19 with Paxlovid (nirmatrelvir plus ritonavir) was safe and reduced the risk of progression to severe Covid-19 by 89% compared to placebo[8]. However, any effect of Paxlovid on long term complications after COVID-19 has yet to be shown.

1.1 Aims and Objectives

The primary objective is to to investigate if early treatment with Paxlovid (nirmatrelvir plus ritonavir) for patients with acute COVID (confirmed PCR or lateral flow test) can reduce long term complications (long COVID).

Long COVID will be defined as one or more of the new-onset symptoms fatigue, dyspnoea and cognitive difficulties.

The secondary objective is to determine whether early COVID treatment with Paxlovid will reduce all-cause, non-elective hospitalisation or death within 28 days of randomisation. Secondary objectives will further include to examine Paxlovid treatment affects time to self-reported recovery; participant reported illness severity; duration of symptoms and symptom recurrence; healthcare service use; participant reported household infection rate; safety outcomes and cost-effectiveness outcomes; symptoms and well-being at six months (with determination of proportion with Long Covid) from randomisation. See Table 1 for details of objectives and outcome measures.

Table 1. Objectives and Outcome Measures

	Objectives	Outcome Measures	Timepoint (s)
Primary	To determine whether Paxlovid treatment in the community reduces risk of long-term complications of COVID-19 (long COVID)	Presence of long-COVID	3 months after randomisation
Secondary	To determine whether Paxlovid treatment in the community safely reduces non-elective overnight hospitalisations/ deaths in symptomatic patients with confirmed COVID-19	All cause, non-elective hospitalisation and/or death, within 28 days of randomisation	Within 28 days of randomisation Participant report, review of health registry data for up to 1 year (Norwegian Patient Registry, Norwegian Pandemic Registry and Norwegian Cause of Death Registry)
	To explore whether Paxlovid treatment affects 1) Time to recovery (defined as the first instance that a participant report of feeling recovered from the illness) 2) Participant reported illness severity, reported by daily rating of how well participant feels, enabling identification of sustained recovery. 3) Duration of symptoms and symptom recurrence	1-3) Participant reported symptoms daily for 7 days, weekly for 28 days and at 3 and 6 months.	1-3) Online participant report daily for 7 days, weekly for 28 days and at 3 and 6 months.
	4) To determine whether Paxlovid treatment in the community safely reduces contacts with the health services	4) Contacts with health services reported by participants and/or	4) Online participant report daily for 7 days, weekly for 28 days and at 3 and 6 months.

		captured by review for health registries	Review of health registry data for up to one year (Norwegian Patient Registry, Norwegian Pandemic Registry and Norwegian Registry for Primary Health Care)
	5) To determine whether Paxlovid treatment in the community safely reduces new infections in household	5) New infections in the household reported by the participants	5) Online participant report day 0 – 6, weekly for 28 days
	6) To investigate the safety of Paxlovid	6) Evaluation of overall safety of drugs by the monitoring of adverse events	6) For the duration of the antiviral course and 3 months after inclusion
	7) To investigate the longer term effects	7) Well-being, symptoms and health care utilisation	7) Online participant report at six months, health registry search for up to one year
	8) To investigate the cost effectiveness	8) Resource use and cost data	8) Baseline, Day 28 and at 3 months.
Exploratory subproject 1. Primary	1) To investigate the relationship between long COVID, neurocognitive dysfunction and alterations in the brain neural connectome.	1) Data from fMRI, EEG and neuropsychological assessment.	1) 3 and 6 months

Secondary	To document long COVID associated changes in 1) The brain volume 2) The brain resting state activity 3) The neural connectome 4) The brain activity during cognitive tasks 5) Cognitive domain functions	 1) Volumetric data from MRI 2) Data from fMRI 3) Diffusion tensor MRI data 4) Alfa and theta frequencies registered with EEG 5) Neuropsychological assessment	 1) 3 and 6 months 2) 3 and 6 months 3) 3 and 6 months 4) 3 and 6 months 5) 3 and 6 months
Exploratory subproject 2 Primary	1) To investigate the relationship between long COVID and persistent inflammation, and identify biological, immune and inflammatory markers		1) study duration up to 12 months
Secondary	1) SARS CoV-2 specific antibodies 2) SARS-CoV-2 specific B cells 3) Markers of immune activation and cellular exhaustion 4) SARS CoV-2 specific T-cell responses 5) phenotyping of leukocyte subsets	1) SARS CoV-2 specific binding and neutralising antibodies 2) SARS-CoV-2 specific B cells by ELISpot and flow cytometry 3) Immune activation, cellular exhaustion, extracellular matrix and markers of impaired blood-brain-barrier function 4) SARS CoV-2 specific T-cell memory and exhaustion responses 5) deep phenotyping	1-5) baseline, 3-12 months

		of leukocyte subsets by mass cytometry,	

1.2 Risk Benefit assessment

The available safety data in the EU risk management plan for paxlovid (pf-07321332/ritonavir) indicates that PF-07321332/ritonavir has a favourable safety profile in the population studied. No safety signals have been identified. PF-07321332/ritonavir was well tolerated for 5 days of dosing in high-risk COVID-19 individuals. Overall, no previously unknown important risks have been identified.

The most important known risk factors are hepatic impairment, and renal impairment, as well as women who are pregnant and lactating. These patients groups are excluded from this study. Any ongoing or new symptoms are systematically collected at all study time points.

Studies to date have not identified any new major risks.

The potential benefit to the participant is early treatment of COVID-19, thereby avoiding serious disease, hospitalisation and death.

2. TRIAL DESIGN AND PROCEDURES

PANORAMIC Norway is a two-arm 1:1 randomized double-blind, placebo-controlled prospective, clinical trial in community care. Trial arms will include:

Intervention arms: The antiviral agent Paxlovid (nirmatrelvir plus ritonavir) in addition to standard of care

Comparator arm: Placebo plus standard of care.

Any use of over-the-counter medication as well as key medications such as inhaled steroids and monoclonal antibodies will be captured, and changing outcomes and treatment modalities over time will be accounted for in the analysis.

2.1 Participant Identification

2.1.1 Trial Participants

The trial includes participants who test positive for SARS-CoV-2 infection, and with ongoing symptoms consistent with COVID-19, who are not hospitalised, and who are aged between 18 years and 65 years of age.

2.1.2 Inclusion Criteria

- Symptoms attributable to COVID-19 started within the past 5 days and ongoing
- Positive PCR or lateral flow SARS-CoV-2 test. Any positive PCR test or a lateral flow test taken between two days before symptom onset and randomisation qualifies.
- Age between 18 and 65 years
- Participant is able and willing to provide informed consent
- Willingness to take a pregnancy test prior to starting study treatment (Participants of childbearing potential)
-

2.1.3 Exclusion Criteria

- Patients that are not able to comply with all study visits
- Patient currently inpatient at hospital
- Comorbidity which requires active antiviral treatment as judged by the investigator
- Any chronic renal impairment
- Any chronic liver disease or liver impairment
- Previous randomisation in the PANORAMIC Norway trial
- Currently participating in a clinical trial of a therapeutic agent
- Currently taking Paxlovid
- Known allergy to Paxlovid
- Use of concomitant medication contraindicated for the treatment of Paxlovid*
- Pregnant and lactating women
- Participants of childbearing potential (participants who are anatomically and physiologically capable of becoming pregnant), or have a partner of childbearing potential, not willing to use highly effective contraceptive until 7 days after completing Paxlovid.

* **Concomitant medications that are contraindicated for the treatment of Paxlovid**

- Medicinal products that are highly dependent on CYP3A for clearance and for which elevated concentrations are associated with serious and/or life-threatening reactions.
- Medicinal products that are potent CYP3A inducers where significantly reduced nirmatrelvir/ritonavir plasma concentrations may be associated with the potential for loss of virologic response and possible resistance.
- Paxlovid cannot be started immediately after discontinuation of any of the following medicinal products due to the delayed offset of the recently discontinued CYP3A inducer.

Medicinal products listed below are a guide and not considered a comprehensive list of all possible medicinal products that are contraindicated with Paxlovid. Further guidance on contraindicated concomitant medication is provided in the SmPC.

- Alpha1-adrenoreceptor antagonist: alfuzosin
- Analgesics: pethidine, piroxicam, propoxyphene
- Antianginal: ranolazine
- Anticancer drugs: neratinib, venetoclax
- Antiarrhythmic: amiodarone, bepridil, dronedarone, encainide, flecainide, propafenone, quinidine
- Antibiotics: fusidic acid, rifampicin

- Anticonvulsants: carbamazepine, phenobarbital, phenytoin
- Anti-gout: colchicine
- Antihistamines: astemizole, terfenadine
- Antipsychotics/neuroleptics: lurasidone, pimozide, clozapine, quetiapine
- Ergot derivatives: dihydroergotamine, ergonovine, ergotamine, methylergonovine
- GI motility agents: cisapride
- Herbal products: St. John's wort (Hypericum perforatum)
- Lipid-modifying agents:
    - HMG Co-A reductase inhibitors: lovastatin, simvastatin
    - Microsomal triglyceride transfer protein (MTTP) inhibitor: lomitapide
- PDE5 inhibitor: avanafil, sildenafil, vardenafil
- Sedative/hypnotics: clorazepate, diazepam, estazolam, flurazepam, oral midazolam and triazolam

2.2 Trial procedures

2.2.1 Recruitment

Potential participants can present directly to the trial team via the trial website or telephone. Dissemination of trial information and recruitment of potential trial participants will commence through several channels:

I. All health professionals (including primary care physicians and Test and Trace staff, pharmacy staff, etc.) will be able to provide information about participation and direct potential participants to the online trial information and the trial website.
II. Media campaigns will use television, radio and social media platforms to generate awareness of the trial and to sign-post to the trial.
III. All facilities including testing centres and municipality centres will be able to inform potentially eligible participants about the trial, and refer them to the trial website and/or trial team.
IV. Clinicians can reach out to potentially eligible participants identified by receiving SARS-CoV-2 test results from Test and Trace and laboratories, and by regular searches for patients with a positive SARS-CoV-2 test result in their clinical database. Contact can be made with potential participants verbally or by text, email, and telephone.
V. PraksisNett, a data extraction service for primary care data, and analogous general practice clinical record facilities, will be able to reach out to potentially eligible participants and signpost them to the PANORAMIC Norway website to explore their participation.

2.2.2 Screening and eligibility

Remote screening and eligibility procedures will be used.
Screening information will be completed during a telephone call with a member of the trial team. A member of the trial team (medically qualified clinician or appropriately trained research nurse) will then confirm eligibility.

Eligibility can be assessed by eliciting medical history and relevant information directly from the participant, and the participant can be randomised if there is no contraindication to the

study drugs currently in the trial. Where necessary, eligibility checking will be assessed additionally through direct access to the participant's Medical Record (or similar medical record summary), or by reference to relevant medical information obtained from the participant's primary care medical practice.

For participants who are too unwell or unable to respond to surveys themselves, a Study Partner who they identify will be able to assist their participant in completing screening, baseline, and follow up online forms and/or calls and provide information to them on their behalf where necessary.

2.2.3 Informed Consent

Eligible participants will be asked to physically attend the study central site for enrolment in the study. Written informed consent will be provided after a two-way discussion between a member of the trial team and the participant, where the risks and benefits of taking part and follow-up procedures will be explained. Adults who lack capacity to consent will not be recruited.

Prior to consent, written and summary versions of the Patient Information Sheet (PIS), and Informed Consent Form (ICF) will be available to participants detailing no less than: the exact nature of the trial; and the known side-effects and risks involved in taking part. It will be clear that the participant is free to withdraw from the study at any time. Adequate time will be given to the participant to consider the information and to ask any questions about the trial before deciding whether to participate.

After informed consent is signed, participants will enter online baseline information, including demographics, comorbidities, concomitant medication, allergies, COVID vaccine history and previous COVID-19, residual symptoms of past COVID-19-infection, as well as their contact details and those of a Study Partner. Identifying a Study Partner is not a requirement of study participation.

2.2.4 Randomisation

A randomisation list will be generated by a qualified person not involved in the trial and forwarded directly to the company producing placebo capsules. Prior to the initiation of the study, the pharmaceutical company performing the encapsulation of the IMPs (Paxlovid and placebo) will assign study IDs to the medicinal packages based on the randomisation list. At inclusion, the trial team will allocate the participants to the next available study ID number and the corresponding Paxlovid/placebo medicinal package. No study procedures will occur until informed consent is signed.

2.2.5 Blinding and code-breaking

PANORAMIC Norway is a double-blinded placebo-controlled trial. If unblinding or code breaking is required, as requested by the protocol or the Data and Safety Monitoring Committee (DSMC) this will be made available to the DSMC. However, those managing the data will be blind to participant allocation.
The trial team and recruiting clinicians will be blinded to emerging results of interim analyses. During the course of the trial, only the unblinding statisticians and the independent members of the DSMC will have access to the unblinded interim results.

2.2.6 Participants of child-bearing potential

For the purpose of this document, a woman is considered of childbearing potential following menarche and until becoming post-menopausal unless permanently sterile. Permanent sterilisation methods include hysterectomy, bilateral salpingectomy and bilateral oophorectomy. A postmenopausal state is defined as no menses for 12 months without an alternative medical cause.

Paxlovid is not recommended during pregnancy and in women of childbearing potential not using contraception unless the clinical condition requires treatment with Paxlovid.

To mitigate the risk of pregnancy in the trial, all participants of child-bearing potential will be required to take a urine pregnancy test prior to commencing trial treatment. Thus, they should indicate willingness to take such a pregnancy test at screening. Before starting the trial treatment the clinician/research nurse will explain to the participant that pregnancy is an exclusion criterion, and explain the contraception requirements during the trial. If the participant confirms that there is a possibility that they may be pregnant during this call, they will be excluded from taking part. The pregnancy test will be supplied in the participant pack with the antiviral agent, for women of childbearing potential. The pregnancy test must be completed prior to starting the trial treatment, and we will confirm a negative test result during the Day 1 telephone call with a member of the trial team.

Highly effective contraception* is advised during the period of medication for women of childbearing potential. All male participants will also be required to use contraception as a precautionary measure for 7 days after completing Paxlovid if they have a partner of childbearing potential. This will be clearly explained prior to randomisation (see section 2.2.7 Follow-up procedures for details regarding confirmation of a negative test result). Use of ritonavir may reduce the efficacy of combined hormonal contraceptives. Patients using combined hormonal contraceptives will be advised to use an effective alternative contraceptive method or an additional barrier method of contraception during treatment with Paxlovid, and until one menstrual cycle after stopping Paxlovid.

Participants themselves will be asked on day 14, day 28, and 3 months ECRF whether they have become pregnant since enrolling into the trial. These responses will be monitored and if a participant does become pregnant during the trial, follow-up information regarding the outcome of the pregnancy and any postnatal sequelae in the infant will be obtained. The CI or delegated individual will liaise with the relevant obstetrician or equivalent healthcare professional throughout the pregnancy until delivery to monitor for congenital abnormality or birth defect, at which the pregnancy would fall under the definition of serious and require reporting as an SAE. The DMSC will be informed of any pregnancies in this treatment group, in weekly safety reports. Pregnancies and outcomes will be included in annual safety reports.

*Highly effective methods have typical-use failure rates of less than 1% and include sterilisation and long-acting reversible contraceptive (LARC) methods (intrauterine devices and implants) OR if a couple are using another method of contraception, such as a combined hormonal method, progestogen only pill or injection, they are only eligible if they are willing to use an additional barrier method (e.g. male condom). Note: a barrier method on its own is not sufficient.

2.2.7 Follow-up Procedures

Follow-up will be via self-completed questionnaires online or through telephone calls.

All patient-related procedures at Day 0 will occur after the informed consent form is signed. After enrolment at the study central site, participants will allocated to receive the trial drug (active ingredient or placebo) according to the randomization list (see section 3.1 Medication Distribution). The participant pack will contain: IMP (the antiviral agent or Placebo), an information booklet; medication card detailing how the medication should be administered, precautions and safety guidance; medication appendix providing further information about the treatment (available prior to randomisation as part of the PIS); emergency contact card; pregnancy test (only for participants of child-bearing potential).

A safety call will be made on Day 1 (day after randomisation) to women of child-bearing potential by a member of the trial team. During this Day 1 call, a member of the trial team will confirm with participants of childbearing potential, that a pregnancy test has been done and that the result is negative before starting the study drug. In the event of a positive test result, the participant will be asked not to take any of the study drug, return it, and will be withdrawn from the trial. Results will be documented in the Day 1 Call CRF. The pregnancy test must be completed prior to taking the study drug and this will be clearly explained prior to randomisation.

All participants, irrespective of group allocation, will be contacted on Day 2 (2 days after randomisation) to confirm follow-up procedures and answer queries. The contact may be either electronic or by phone. At this day 2 contact, compliance will be assessed and participants will be also asked if they are experiencing any potential side-effects.

Participants on all arms of the trial will complete an electronic diary each day for 7 days, weekly for 28 days, and then at 3, 6, and 12 months from randomisation, where they will rate the severity of symptoms, record contacts with the health services (including hospital admissions, hospital outpatient visits, accident and emergency attendances, use of specialist services and primary care encounters), impact of symptoms on work/study, record study medication use and new infections in the household. We will collect the Chalder fatigue scale questionnaire and specific questions capturing relevant symptoms. Participants will be contacted at three and six months to ascertain wellbeing and longer-term consequences of their illness, including proportion with long Covid.

The trial team will retrospectively retrieve relevant information from hospital records, Norwegian health registries, for example details concerning COVID-related hospital admittance (Norwegian Pandemic Registry), mortality and cause of death (Norwegian Cause of Death Registry), contacts with primary care (Norwegian Registry for Primary Health Care (KPR), COVID vaccine history (Norwegian Immunisation Registry (Sysvak)), drug prescription (Norwegian Prescription Database (NorPD), Norwegian Surveillance System for Communicable Diseases (MSIS) and sick leave (The Sickness Absence Registry).

To investigate the impact of trial interventions on the longer-term effects of COVID-19, we will also remotely follow-up participants, for up to 1 year.

The research team will call participants/study partners with no internet access or those who have not completed their diary for at least two days before day 7. No more than two contact attempts will be made at each of these follow-up points. There will be a participant phone number accessible on weekdays. The municipality emergency facility (Legevakt), and the Emergency department of local hospitals will be made aware of the study and have contact information to study medical personnel. Study participants will be informed that they can at any time withdraw from the study.

2.2.8 Exploratory subgroup studies

A subgroup of up to 500 patients will be asked to attend a face-to-face visit or to donate a microbiological and/or blood sample for the purpose of the study, and to undergo neurocognitive testing and fMRI investigations, at 3, 6 and 12 months after inclusion.

Exploratory Subprojects:

1. **Study on brain damage in long COVID.**

Hypothesis: Neuroimaging can identify brain structural or functional damage in long COVID patients that correlate with neuropsychological deficits. This project will include 50 patients without symptoms at 3 months and 50 patients with cognitive symptoms at 3 months, and they will be followed at 3-, 6- and 12-months post infection. **Exploratory endpoints:** Document the hypothesized relationship between long COVID, neurocognitive dysfunction and alterations in the brain neural connectome of patients with acute SARS-CoV-2 infection at 3- and-6-month time-points. The exploratory secondary outcomes will be (i) loss of brain volume assessed with volumetric MRI; (ii) reduced resting state activity evaluated with fMRI; (iii) quantified reduction in the neural connectome using diffusion tensor MRI; (iv) persistent slowing of brain activity registered with EEG in the alfa and theta frequencies at rest and during cognitive tasks; (v) quantification of cognitive domain functions with neuropsychological assessment.

Data to be recorded Changes in brain volume, and density of white matter fiber tracts. Changes in brain activity using resting state fMRI and EEG registration at rest and during cognitive tasks. Document deficits in memory, spatial navigation, cortical motor control, concentration and focus control, mental endurance and affective processing.

2. **Immune profiling of COVID-19 patients with no or COVID sequalae.**

Hypothesis: Long COVID appears to be a state of immune dysfunction that involves persistent inflammation, and identification of biological, immune and inflammatory parameters of this dysfunction will reveal potential additional targets for intervention, risk prediction and prevention.

Methods: Biological samples such as blood and respiratory samples will be collected during the acute phase and convalescent phase at appropriate time periods with possible follow up to 12 months. From the same group of 100 patients in subproject 1, supplemented with up to 400 additional patients to a total of maximum 500 participants, follow-up blood samples will be collected to allow detailed immune profiling. Serum, EDTA plasma and PaxGene tubes will be collected (up to 50 ml). In a subset of subjects, peripheral blood mononuclear cells will be collected up to 50ml of blood. We will correlate SARS CoV-2 specific B-and-T cell functions and changes in inflammatory and immune markers with the severity of long COVID. We will

conduct state of the art immunological assays using established protocols to investigate (i) SARS CoV-2 specific binding and neutralising antibodies to SARS CoV-2 variants using ELISA and neutralisation assays (ii) Detection of SARS-CoV-2 specific B cells by ELISpot and flow cytometry, including deciphering B cell receptor signaling and recall responses in SARS CoV-2 antigen specific B lymphocytes. (iii) Markers of immune activation/cellular exhaustion (e.g., TIM-3/LAG-3/CEACAM1), cellular senescence/accelerated aging (e.g., chitotriosidase and stathmin1), extracellular matrix remodeling (e.g., GDF-15 and osteopontin), vascular inflammation (e.g., von Willebrand Factor, CXCL16 and pentraxin-3) and markers of impaired blood-brain-barrier function (e.g., MADCAM, NCAD) will be measured by high-throughput ELISA in all participants during follow-up. Proteomics in serum plasma (OLINK Explore panel, >1500 analyses) and RNA sequencing and targeted/untargeted proteomic (Mass Spectrometry) on immune cells will be used as discovery platforms that among others will include analyses of DNA repair mechanisms and mitochondrial function as well as epigenetic and epitransciptomic modifications . (iv) SARS CoV-2 antigen specific T-cell responses including memory and exhaustion markers and SARS-CoV-2 Spike specific CD4+ T cells will be assessed by ELISpot and multiparametric flow cytometry**,** (v) deep phenotyping of leukocyte subsets by mass cytometry, including T and B cells, monocyte, dendritic cells and NK cell subsets.

3. Comparison to the UK PANORAMIC study

The following comorbidities will specifically be identified:

- chronic respiratory disease (including chronic obstructive pulmonary disease (COPD), cystic fibrosis and asthma requiring at least daily use of preventative and/or reliever medication)
- chronic heart or vascular disease
- chronic kidney disease
- chronic liver disease
- chronic neurological disease (including dementia, stroke, epilepsy)
- severe and profound learning disability
- Down's syndrome
- diabetes mellitus (Type or Type II)
- 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, human immunodeficency virus (HIV), cancer, chemotherapy)
- solid organ, bone marrow and stem cell transplant recipients
- morbid obesity (body mass index (BMI) >35)
- severe mental illness

2.3 Economic evaluation

A prospective economic evaluation will be embedded within the trial design to assess the cost effectiveness of Paxlovid[9]. We will estimate the resource inputs associated with embedding Paxlovid treatment into routine clinical practice, and estimate societal costs. Broader resource use will be drawn from General Practice Data (PraksisNett) and linked Hospital Episode Statistics – encompassing primary care encounters, hospital inpatient/day case admissions, outpatient visits, and accident and emergency attendances. Unit costs will be valued using national reference tariffs and attached to resource inputs to generate a compound total health care cost per trial participant over the trial time horizon. Secondary expressions of cost-

effectiveness will include incremental cost per hospitalization and/or death prevented over 28 days and 3 months.

Bivariate regression of costs and measures of health consequence, with multiple imputation of missing data, will be conducted to generate within-trial estimates of incremental cost-effectiveness. Sensitivity analyses will assess the impact of areas of uncertainty surrounding components of the economic evaluation. Cost-effectiveness acceptability curves will show the probability of cost-effectiveness of each treatment evaluated at alternative cost-effectiveness thresholds. Cost-effectiveness threshold values will be informed by guidance from Norwegian government departments on the value placed by decision-makers on an additional QALY[10] and on a statistical life[11].

A decision-analytic modelling-based economic evaluation will also be conducted. The baseline decision-analytic model will be developed during the early stages of the study, and aim to provide a framework for extrapolating the cost-effectiveness of each antiviral beyond the parameters of PANORAMIC Norway trial. Accepted guidelines for good practice in decision-analytic modelling will be followed. The model will consider the progression of symptomatic COVID-19 status over time, and the model structure will capture disease progression using health states that represent the important natural history and clinical- and event-related activity for symptomatic COVID-19 symptomatic status, the appropriate model type (e.g. Markov or discrete-event simulation approach) and the appropriate analytical framework (e.g. cohort analysis versus individual-level simulation). Parameter inputs into the model will be informed by data extracted from PANORAMIC Norway trial, supplemented by data identified from external sources following targeted literature searches. As with the within-trial economic evaluation, cost-effectiveness will be expressed in terms of incremental cost per QALY gained. Multi-parameter uncertainty in the model will be addressed using probabilistic sensitivity analysis. Cost-effectiveness acceptability curves will be used to show the probability of cost-effectiveness of each anti-viral strategy at alternative cost-effectiveness thresholds held by decision-makers. Long-term costs and health consequences will be discounted using nationally recommended discount rates. Specific plans for the economic evaluation will be outlined in a pre-specified health economics analysis plan.

2.4 Early Discontinuation/Withdrawal of Participants

Each participant has the right to withdraw from the study at any time. In addition, the Investigator may discontinue a participant from the study at any time if the Investigator considers it necessary for any reason including:

- Ineligibility (either arising during the study or retrospectively)
- Withdrawal of consent

The reason for withdrawal will be recorded. Data that has already been collected about the participant will be kept and used in the analyses of the trial. Withdrawn participants will not be replaced.

2.5 Definition of End of Trial

The end of the trial will be the timepoint for last controlled data capture of last participant.

2.6 Early termination

The sponsor reserves the right to terminate the study at any time for any reason at the sole discretion of the sponsor.

Further reasons for early discontinuation of the study may include:

- Major safety concerns are revealed by the DSMC based on the interim-analysis or SAE/SUSAR reports.
- Following a serious breach
- Inadequate or no recruitment (evaluated after a reasonable amount of time) of participants by the investigator
- Withdrawal of funding or study medication

If the study is prematurely terminated or suspended, the sponsor shall promptly inform the investigators and the regulatory authorities of the reason for termination or suspension. The investigator shall promptly inform the participant and assure appropriate participant therapy and/or follow-up.

3. TRIAL INTERVENTIONS

3.1 Study interventions administered

IMP: Paxlovid / placebo
Participants will be randomised to Paxlovid or Placebo for five days. Randomisation will be performed by an external statistician prior to the study, by sending the randomisation list to the placebo producer where encapsulation of both intervention drug and placebo is performed. The placebo producer will label the containers of Paxlovid and placebo with numbers according to the randomization list.

Dose
1 dose Paxlovid contain 2x150 mg nirmatrelvir + 100 mg Ritonavir. In this study the tablets are encapsulated to maintain blinding.

2x150 mg nirmatrelvir + 100 mg Ritonavir for oral administration twice daily (every 12 hours) for 5 days

3.2 Preparation, Handling, Storage, and Accountability

a. Encapsulation and labelling

Kragerø tablettproduksjon AS, Kirkegata 15, 3770 Kragerø will encapsulate and label the IMP for trial purposes in accordance with Annex 13.

b. Medication Distribution

Distribution of trial packs to participants will be performed at the central site at the time of enrolment (with appropriate infection control measures).

c. Storage

Will be stored below 25 °C. Should not be refrigerated or freezed. Will be stored securely at clinical site with restricted access.

d. Drug accountability

Accountability logs will be kept by the distributor, study pharmacy and the study site, central monitoring of the logs will allow oversight by the study monitor.

e. Drug Destruction/Returns

Participants will receive IMP for 5 days treatment. Participants withdrawing for trial treatment prior to completing the 5 day treatment period be asked to return unused IMP to the site by post or in person. Unused study medication will be destroyed by an authorised third party.

3.3 Medication adherence

A safety call will be made to all participants on day 2 to ensure compliance and that the medication is used as prescribed. Moreover, medication adherence will be captured daily in the electronic diaries or in phone calls with the patient. The research team will call participants/study partners who have not completed their diary for at least two days before day 7. No more than five contact attempts will be made at each of these follow-up points. Deviation(s) from the prescribed dosage regimen will be recorded.

3.4 Overdose

Treatment of overdose with Paxlovid should consist of general supportive measures including monitoring of vital signs and observation of the clinical status of the patient. There is no specific antidote for overdose with Paxlovid.
We will monitor potential overdoses by asking in the daily diary Day 1 – 7 whether the participant has taken more than the specified dose. A safety alert will be triggered if the participant records that they have exceeded the dose. A Doctor from the central clinical team will contact the participant immediately and follow-up accordingly, with a minimum of daily telephone calls for 7 days to monitor any potential AEs caused by the overdose.

4. SAFETY REPORTING

Symptoms, adverse events and Serious Adverse Events (SAE) will be collected from participant daily diaries, as well as calls to participants/Study Partners.

We will adopt a risk assessed and proportionate approach to safety monitoring. In line with the SmPC, we will assess the risks and the safety profile, and detail the mitigation and monitoring procedures. All safety procedures will be according to NorCRINs standard operating procedures (Safety Reporting SOP).

a. **Reference Safety Information (RSI)**

Current SmPC will be RSI for this trial

Hazard	Likelihood (L,M,H)	Impact (L,M,H)	Mitigation	Monitoring
1. Pregnancy: i. Potential teratogenicity ii. There are no human studies of use among pregnant or lactating people.	H	H	Requirement for negative pregnancy test in participants of child-bearing potential, prior to starting medication. We will exclude known pregnancy, breastfeeding, and require participants to use adequate contraception for the duration of the treatment and 7 days of follow-up, including participants with a partner with child bearing potential. During the pre-randomisation call, the clinician/research nurse will confirm this exclusion criteria with the participant.	Confirmation of negative pregnancy test documented in the Day 1 and/or Day 2 Call CRFs and Daily Diary We will monitor daily responses to the question 'have you become pregnant since starting the trial?' and follow-up as required to immediately stop treatment, if applicable. Pregnancy occurring during the 28-day trial follow-up period will be reported as an AE of Special Interest. As per CTU SOP Pharmacovigilance, any pregnancy that occurs during IMP administration requires monitoring and follow-up until the outcome of the pregnancy is known. The CI or delegated individual will liaise with the relevant Obstetrician throughout the pregnancy. The DMSC will be informed of any pregnancies in this treatment group, in weekly safety reports.
2. Unknown/other potential side-effects	M	M	All participants will receive a call on day 1 to make sure that they understand the possible risks associated with Paxlovid and how to report potential side-effects and seek medical care if required. Participants will be provided with a 24 hour contact telephone line to report any AEs that they experience and are concerned about, directly to a clinician. We will collect symptoms and side effects from symptom	The DMSC will review weekly reports of unblinded symptom data to identify potential side-effects of Paxlovid. Any safety signals will be communicated to the TSC and TMG. The TMG will monitor SAEs, AEs and calls to the 24hr safety phone line, for potential safety signals,

			diaries and participant telephone calls.	
3. Compliance			Participants will be asked in their daily diaries about trial medication use	The trial team will monitor daily diary responses where the participant indicates that they have taken too much IMP, and escalate to the clinical team to follow-up with the participant.

4.1 Procedures for Reporting Adverse Events (AE) and Serious Adverse Events

The participant will be asked to rate the severity of a number key COVID-19 symptoms which are also possible common medication side effects in their daily diary. Symptoms of COVID-19 and medication adverse event symptoms may overlap and can be difficult to disentangle. Trends in the prevalence in the severity of symptoms between Placebo/Usual Care and Paxlovid arms will be compared, for evidence of increased severity of measured symptoms in those randomised to receive Paxlovid.

i. AE reporting

AE Definition

- An AE is any untoward medical occurrence in a clinical study participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention.
- NOTE: An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of study intervention.

AEs will be monitored from the start of treatment for 12 months, and assessed by a clinician (independent from the Sponsor) for causality and severity (definitions below).

Participants will be free to withdraw from taking the IMP if they perceive they have an intolerable AE. Participants will also be provided with a Trial Wallet Emergency Card detailing potential side-effects and a contact telephone line, answered by a clinical team, enabling them to report AEs they experience whilst taking the drug. This card will also alert hospital clinicians about trial participation, should a participant be admitted to hospital. In the event of a medical emergency, trial participants will be instructed to show this card to the clinician they see. Based on clinical judgement, the clinician may contact the participant directly within 24 hours of becoming aware of an AE reported in their daily diary or on the study-specific telephone number, to advise the participant on the appropriate clinical care.

ii. AE Severity Assessment (for assessing clinician)

Clinical assessment of severity

GRADE 1 (Mild)	Short-lived or mild symptoms; medication may be required. No limitation to usual activity
GRADE 2 (Moderate)	Moderate limitation in usual activity. Medication may be required.
GRADE 3 (Severe)	Considerable limitation in activity. Medication or medical attention required.

iii. SAEs

Definition of SAE

An SAE is defined as any untoward medical occurrence that, at any dose, meets one or more of the criteria listed:

a. Results in death

b. Is life threatening

The term *life threatening* in the definition of *serious* refers to an event in which the participant was at risk of death at the time of the event. It does not refer to an event, which hypothetically might have caused death, if it were more severe.

c. Requires inpatient hospitalization or prolongation of existing hospitalization

- In general, hospitalization signifies that the participant has been admitted (usually involving at least an overnight stay) at the hospital or emergency ward for observation and/or treatment that would not have been appropriate in the physician's office or outpatient setting. Complications that occur during hospitalization are AEs. If a complication prolongs hospitalization or fulfills any other serious criteria, the event is serious. When in doubt as to whether hospitalization occurred or was necessary, the AE should be considered serious.
- Hospitalization for elective treatment of a pre-existing condition that did not worsen from baseline is not considered an AE.

d. Results in persistent or significant disability/incapacity

- The term disability means a substantial disruption of a person's ability to conduct normal life functions.
- This definition is not intended to include experiences of relatively minor medical significance such as uncomplicated headache, nausea, vomiting, diarrhea, influenza, and accidental trauma (e.g. sprained ankle) that may interfere with or prevent everyday life functions but do not constitute a substantial disruption.

e. Is a congenital anomaly/birth defect

f. Other situations:

- Medical or scientific judgment should be exercised by the investigator in deciding whether SAE reporting is appropriate in other situations such as important medical events that that may not be immediately life-threatening or result in death or hospitalization but may jeopardize the participant or may require medical or surgical intervention to prevent one of the other outcomes listed in the above definition. These events should usually be considered serious.

- Examples of such events include invasive or malignant cancers, intensive treatment in an emergency room or at home for allergic bronchospasm, blood dyscrasias, convulsions not resulting in hospitalization, or development of intervention dependency or intervention abuse.

Definition of suspected unexpected serious adverse reaction (SUSAR)
If an event is not an SAE per definition above, then it cannot be a SUSAR

SUSAR Definition

Adverse Reaction: all unwanted and unintended responses to an investigational medicinal product related to any dose administered.

Unexpected Adverse Reaction: an adverse reaction, the nature or severity of which is not consistent with the applicable product information.

Suspected Unexpected Serious Adverse Reaction: Unexpected Adverse Reaction that:

- Results in death
- Is immediately life-threatening
- Requires in-patient hospitalization or prolongation of existing hospitalization
- Results in persistent or significant disability or incapacity
- Is a congenital abnormality or birth defect

Is an important medical event that may jeopardize the subject or may require medical intervention to prevent one of the outcomes listed above.

All-cause hospitalisation and death are secondary outcomes, and this data will be captured in CRFs. SAEs other than hospitalisation or death due to COVID-19 must be reported for Paxlovid.

SAEs must be reported to sponsor by the person who has discovered the SAE or nominated delegate within 24 hours of becoming aware of the event. Some SAEs occurring within the 28-day follow-up period, may be identified retrospectively from data extracts and not in real-time. These will be reported within 24 hours of becoming aware of the event. The sponsor or delegate will ensure it is reviewed by the medical monitor or other delegated personnel for relatedness and expectedness as soon as possible taking into account the reporting time for a potential SUSAR according to the relevant competent authority. If the event has not resolved, at the 28-day time point the SAE will be reviewed again by the central clinical team, to see if resolution has occurred. If the event is considered 'resolved' no further follow up is required. If not, the event must be followed up until such a time point.

All SAEs that have not resolved by the end of the study or those that are identified retrospectively, or that have not resolved upon discontinuation of the participant's participation in the study, must be followed until any of the following occurs:

• The event resolves
• The event stabilises
• The event returns to "baseline", if a "baseline" value/status is available
• The event can be attributed to agents other than the study intervention or to factors unrelated to study conduct
• It becomes unlikely that any additional information can be obtained (participant or health care practitioner refusal to provide additional information, lost to follow-up after demonstration of due diligence with follow-up efforts)

See Appendix C. Supplementary Material for definitions of adverse events

4.1.1. Other events exempt from immediate reporting as SAEs

Hospitalisations will be defined as at least a one-night admission to hospital. Hospitalisation for a pre-existing condition, including elective procedures planned prior to study entry, which has not worsened, does not contribute to the secondary outcome and does not constitute a SAE.

4.1.2. Procedure for immediate reporting of Serious Adverse Events

- Trial team/responsible clinician/CI will complete an SAE report form, directly into the database, for all reportable SAEs.
- The trial team/RCGP will provide additional, missing or follow up information in a timely fashion.
- If necessary, the participant may be contacted to provide additional, missing or follow up information as required.

An investigator, will review the SAE once reported, collect as much information and report to the Sponsor delegate within the timeframe according to the NorCRINs Standard Operation Procedures (SOPs).

4.1.3 Expectedness

For SAEs that require reporting, expectedness of SAEs will be assessed and determined by the Medical Monitor who is unblinded, according to the relevant Reference Safety Information (RSI) section of the Summary of Product Characteristics. The RSI will be the current NoMA/EMA approved SmPC version at the time of the event occurrence.

4.1.4 Assessment of Causality

The relationship of each serious adverse event to Paxlovid must be determined by a medically qualified individual according to the following definitions:

- **Unrelated** – where an event is not considered to be related to Paxlovid
- **Possibly** – although a relationship to Paxlovid cannot be completely ruled out, the nature of the event, the underlying disease, concomitant medication or temporal relationship make other explanations possible.
- **Probably** – the temporal relationship and absence of a more likely explanation suggest the event could be related to Paxlovid.
- **Definitely** – the known effects of Paxlovid, its therapeutic class or based on challenge testing suggest that Paxlovid is the most likely cause.

The investigator will make the assessment of causality.
AEs/SAEs judged possibly, probably or definitely related will be considered as related to the antiviral agent.

4.2 SUSAR Reporting

All SUSARs will be reported by the sponsor delegate to the relevant Competent Authority and other parties as applicable. The period for the reporting of suspected unexpected serious

adverse reactions by the sponsor to the Agency shall take account of the seriousness of the reaction and shall be as follows:
(a) in the case of fatal or life-threatening suspected unexpected serious adverse reactions, as soon as possible and in any event not later than seven days after the sponsor became aware of the reaction;
(b) in the case of non-fatal or non-life-threatening suspected unexpected serious adverse reactions, not later than 15 days after the sponsor became aware of the reaction;
(c) in the case of a suspected unexpected serious adverse reaction which was initially considered to be non-fatal or non- life threatening but which turns out to be fatal or life-threatening, as soon as possible and in any event not later than seven days after the sponsor became aware of the reaction being fatal or life-threatening.

4.3 Annual Report

The Annual report be developed and submitted annually 60 days after the anniversary date that the trial receives Clinical Trial Authorisation. Due to the nature of this trial and the importance of sharing the science of COVID-19 and the drug, internationally, we expect to produce reports to the Norwegian Government and regulatory agency more frequently upon request.

5. STATISTICS

5.1 Statistical Analysis Plan (SAP)

Details of the statistical design and methods for the PANORAMIC Norway trial and are described in the Statistical Analysis Plan (SAP version 1.0, dated 28.2.2023).

5.2 Research hypothesis

Antiviral treatment of acute Covid can prevent occurrence of persisting symptoms at 3 months and beyond.

5.3 Outcome definitions

A total of 13 symptoms will be recorded. The following symptoms are recorded as binary variables: fever, tingling sensation, headache, dizziness, altered taste/smell, sleep disturbances, chest-pain, muscle/joint pains, nausea. The following will be recorded as graded symptoms (better than usual, as usual, worse than usual, much worse than usual): fatigue, dyspnea, memory problems, concentration problems, feeling depressed. Additionally, we will record, absence from work/school (number of days), hospitalization (number of days), any contact with doctor / emergency clinic.

5.3.1 Primary efficacy endpoints

The primary outcome is a dichotomous variable for presence of any of the three most important long-COVID symptoms: (i) fatigue, (ii) dyspnea and (iii) cognitive symptoms (defined as memory and/or concentration problems). The outcome is coded 1 for the presence of any one or more of these 3 symptoms, and 0 for absence of all the 3 symptoms. The primary outcome will first be evaluated at 3-months follow-up, and then re-evaluated at 6-, 12- and 24-months follow-up.

5.3.2 Secondary endpoints

Secondary outcomes include assessment of the intervention's effect on:

- All individual symptoms separately, and grouped by systems (systemic symptoms, chest-symptoms, cognitive, other neuropsychiatric symptoms).
- Graded responses for separate symptoms and symptom constellations, including an ordinal variable graded 0-3 for the presence of the 3 symptoms in the primary outcome.
- Severity of acute disease using an 8-step scale (ref: Beigel, NEJM) (score)
- Hospitalization (binary)
- Mortality at three months (binary)
- Severe adverse events (binary)
- Absence from work (binary)
- Societal cost / economic analysis, including estimated cost of absence from work/school, hospitalizations, deaths, QALYs lost according to EQ-5D-5L, and more.

5.4 Randomization and allocation

Participants will be randomized to antiviral treatment or placebo using fixed equal allocation ratios. An external statistician will produce a randomization list that will be given to the pharmaceutical company packaging interventional drugs and placebo. The active drugs and placebos will be coated by the company so that they look identical, and packages will appear identical. Packages will be labeled with the ID number on the randomization list and patients will be allocated with this ID number. At the time of inclusion in the study, study personnel will blindly allocate participants to receive active ingredient or placebo according to the randomization list.

5.5 Primary Analysis Population

The primary analysis will be an "intention to treat" analysis performed on all patients who were allocated to receive the investigational medicinal product according to the randomisation list. In addition, per protocol analysis will be performed for patients who reported to have adhered to the ingestion of the study product (antiviral or placebo), and on other subgroups of the study population. If adherence is incomplete, we will attempt to estimate the biological effect of the medication by using instrumental variable analysis.

5.6 Withdrawal / follow-up

Participation is based on informed voluntary consent. Participants may withdraw at any time of the study without giving reasons or justification. Upon withdrawal, no further data will be collected. However, data recorded up until the time of withdrawal will be included in the analysis.

5.7 Analysis methods

The primary outcome, i.e. the effect of intervention on a binary variable for the presence of any of 3 key long-COVID symptoms, will be analyzed with an appropriate logistic regression model. Depending on whether we obtain a good balance of prognostic factors between the randomized groups, we may consider adjustment for prognostic factors in the analyses. We will typically report an odds ratio with 95% confidence intervals and a p-value from this analysis.

In the analysis of follow-up data up to 24 months, we will use appropriate mixed models to account for correlation of symptoms over time. We will estimate the main effect of treatment and test whether the effect is uniform over time.

Secondary outcomes will be analyzed with appropriate regression models depending on the type of outcome variable. For binary outcomes, we will use logistic regression. For number of symptom counts, we will consider negative binomial regression and for score outcomes we will attempt ordinal logistic regression and quantile regression. Using quantile regression models, we will estimate the effect of the intervention also in the tails of the score-distribution.

Further analysis plans include cost-efficacy analyses and explorative analyses. We will estimate the resource inputs associated with providing the antiviral treatment in routine clinical practice. Societal costs will be estimated using data on primary care encounters, hospital inpatient/day case admissions, outpatient visits, and accident and emergency attendances. Loss of quality-adjusted life year (QALY) will be estimated. Unit costs will be valued using national reference tariffs. Compound total health care cost per trial participant over the trial time horizon will be estimated. Secondary expressions of cost-effectiveness will include incremental cost per hospitalization and/or death prevented over 28 and 60 days. Relevant data may be obtained from registries, including emergency hospitalization events (Norwegian Patient Registry (NPR)) and Norwegian Pandemic Registry (NIPaR), mortality and cause of death (Norwegian Cause of Death Registry), contacts with primary care (Norwegian Registry for Primary Health Care (KPR)), drug prescription (Norwegian Prescription Database (NorPD) and sick leave (The Sickness Absence Registry). Cost-effectiveness will be expressed in terms of incremental cost per QALY gained.

Bivariate regression of costs and measures of health consequence, with multiple imputation of missing data, will be conducted to generate within-trial estimates of incremental cost-effectiveness. Sensitivity analyses will assess the impact of areas of uncertainty surrounding components of the economic evaluation. The probability of cost-effectiveness at alternative thresholds will be measured. Cost-effectiveness threshold values will be informed by guidance from government departments on the value placed by decision-makers on an additional QALY10 and on a statistical life.

Statistical analysis will be performed in Stata version 17 (StataCorp LLC, College Station, Texas) and R version 4.2.2 or higher (The R Foundation for Statistical Computing, Vienna, Austria). All the relevant regression models are fully implemented in Stata. If imputation is considered necessary or useful, regression analysis with multiple imputation will be performed in Stata using the mi-command. Mixed effects models analysis in R will be performed using the “lme4” or “lmerTest” packages, and imputation will be performed using the mice.impute.bygroup function in the “mice” and “miceadd” libraries in R. We will develop scripts in both systems and check the results for consistency.

5.8 Reporting of statistical results

Analysis results for the primary outcome will be reported as odds ratio with 95% confidence interval with P-value. The standard cut-off of $p<0.05$ will be used for statistical significance levels. For secondary outcomes we will report appropriate effects measures with 95% confidence intervals without p-values. Type I error will be controlled at the traditional 0.05

two-sided level for the hypothesis test. We will perform a hypothesis test only for the primary outcome and we will not need to adjust for multiple tests.

5.9 Sample size justification

We expect to be able to recruit around 2000 patients for randomization in the Norway study. The presence of long covid is our primary endpoint. Prior knowledge suggest that long covid may be present among approximately 50% of the patients. With a total sample size of around 2000 we will be able to detect a 16% treatment effect with a power of 90% (5% significance level, Table 1x). If the prevalence of long covid drops to 40% or 30% in the placebo-group, we will still have 90% power to detect a 17.5% or 21.7% treatment effect, respectively, with a total sample size of approximately 2000.

Table 1x: Sample size scenarios

90% power and 5% significance level, two-sided test of superiority				
Placebo*	**Treatment***	**Treatment effect**	**NNT**	**Total sample size**
50%	42.5%	16%	14	1908
40%	33%	17.5%	15	2042
30%	23.5%	21.7%	16	2008

* Expected prevalence of primary outcome

5.10 Interim analysis and stopping guidance

Interim analysis will be performed when 1000 patients have reached 28 days follow-up assessing any deaths and hospitalizations occurring in the study population.
The study will be stopped if the proportion of deaths at 28 days follow-up is higher in one of the groups by a significance of $p<0.02$ and effect size of odds ratio > 4.

Severe adverse events will be reported consecutively to the DSMB. The DSMB will evaluate this independently of the interim analysis.

5.11 Procedures for Reporting Unplanned Deviation(s) from the Master Statistical Analysis Plan

Any deviations from the protocol will be documented in a protocol deviation form and filed in the study master file. A NorCRIN SOP is in place describing the procedure for identifying non-compliances, escalation to the central team and assessment of whether a non-compliance /deviation may be a potential Serious Breach. Analyses will be carried out in accordance with the SAP. Any additional analysis that is not specified in the SAP or any unplanned deviation(s) from the SAP will be specified in the Statistical Analysis Report. Reasons for these changes will be documented and authorized by the Chief Investigator.

6. DATA MANAGEMENT

The data management aspects of the study are summarised here with details fully described in the Data Management Plan.

6.1 Source Data

Source documents are where data are first recorded. CRF entries will be considered source data where no other primary record is documented. The trial team will use Norwegian health registries as source data for relevant medical information, including emergency hospitalization events (Norwegian Patient Registry (NPR)), details concerning COVID-related

hospital admittance (Norwegian Pandemic Registry), mortality and cause of death (Norwegian Cause of Death Registry), contacts with primary care (Norwegian Registry for Primary Health Care (KPR)), COVID vaccine history (Norwegian Immunisation Registry (Sysvak)), drug prescription (Norwegian Prescription Database (NorPD), Norwegian Surveillance System for Communicable Diseases (MSIS) and sick leave (The Sickness Absence Registry).
Data collected will include participant identifiable information and will be accessed at the Haukeland University Hospital/ University of Bergen according to CTU Information Governance policies and Norwegian GDPR. Data will only be held for the duration it is required; this will be reviewed annually.

All documents will be stored safely in confidential conditions. On all study-specific documents, other than the signed consent, the participant will be referred to by the study participant number/code, not by name.

6.2 Access to Data

Direct access will be granted to authorised representatives from the Sponsor, host institution, and the regulatory authorities to permit trial-related monitoring, audits and inspections.

6.3 Data Recording and Record Keeping

The Investigators will maintain appropriate medical and research records for this trial, in compliance with the requirements of the Clinical Trials Regulation, no. 536/, ICH E6 GCP and regulatory and institutional requirements for the protection of confidentiality of volunteers. The Chief Investigator, Principal Investigator, Co-Investigators, clinical team, including Study Nurses, and other authorised members of the trial team will have access to records. The Investigators will permit authorised representatives of the sponsor, and regulatory agencies to examine (and when required by applicable law, to copy) clinical records for the purposes of quality assurance reviews, audits and evaluation of the study safety and progress.
The data will be entered into CRFs in an electronic format by the participant, trial Partner, or trial team using the secure cloud hosted SAFE server located at the University of Bergen, Norway. Data will be entered in a web browser and then transferred to the database by encrypted (Https) transfer. This includes safety data, laboratory data and outcome data. Safety data will be collected through electronic diaries. Risks are mitigated using the ISO97001 framework.
An online secure data entry system designed to collect sensitive data, such as participant and Study Partner contact details, will be used. All identifiable participant data is encrypted. The participant portal will also manage electronic patient reported outcome data. Participant and Trial Partner data will be kept and stored securely for as long as it's required by the study and reviewed on annual basis.

7. QUALITY ASSURANCE PROCEDURES

The study will be conducted in accordance with the current approved protocol, ICH-GCP, relevant regulations and NorCRIN SOPs. All investigators, coordinating centre staff and site staff will receive training in trial procedures according to ICH-GCP where required. Regular monitoring will be performed according to ICH-GCP using a risk-based approach. Data will be evaluated for compliance with the protocol and accuracy in relation to source documents where possible.

The NorCRIN-CTU Trial Management Group will be responsible for the monitoring of all aspects of the trial's conduct and progress and will ensure that the protocol is adhered to and that appropriate action is taken to safeguard participants and the quality of the trial itself. The TMG will be comprised of individuals responsible for the trial's day to day management and will meet regularly throughout the course of the trial.

7.1 Risk assessment and Monitoring

A risk assessment and monitoring plan will be prepared before the study opens and will be reviewed as necessary over the course of the study to reflect significant changes to the protocol or outcomes of monitoring activities. Monitoring will be performed by the monitors from NorCRIN. The level of monitoring required will be informed by the risk assessment.

7.2 Trial committees

The responsibilities of each group are as follows:

- Data and Safety Monitoring Committee (DSMC) will review the data received from the SAC at each interim analysis as described in the Statistical Analysis section, in order to ensure that the process is working correctly and to review and monitor the accruing data to ensure the rights, safety and wellbeing of the trial participants. Composition, and roles and responsibilities of the DSMC are detailed in the DSMC charter. The DSMC reviews data from interim analyses and makes recommendations to the TSC if safety concerns have emerged.
- Trial Steering Committee (TSC) will ensure the rights, safety and wellbeing of the trial participants. They will make recommendations about how the study is operating, any ethical or safety issues and any data being produced from other relevant studies that might impact the trial. Composition, and roles and responsibilities of the TSC are detailed in the TSC charter. The TSC advises the TMG about the conduct of the study and stopping randomisation to study arms (based on recommendations received from the DSMC and/or relevant information external to the trial). If national recommendations in standard of care changes during the study period, the TSC will make recommendations to the TMG regarding potential new risks or benefits.
- The Statistical Analysis Committee (SAC) will perform interim analysis and report these to the DSMC. The TMG will remain blind to these interim analyses until a recommendation is received form the TSC about stopping randomisation or safety concerns.
- Trial Management Group (TMG) – will be responsible for the day-to-day running of the trial, including monitoring all aspects of the trial and ensuring that the protocol is being adhered to. It will include Co-Investigators and will meet weekly in the first instance. Composition, and roles and responsibilities of the TMG are detailed in the TMG charter.
- A core project team (PT) from within the TMG will meet weekly or as required for operational decision making (meet daily at the start of the trial).

8. PROTOCOL DEVIATIONS

A study related deviation is a departure from the ethically approved study protocol or other study document or process (e.g. consent process or administration of study intervention) or from Good Clinical Practice (GCP) or any applicable regulatory requirements. Any deviations

from the protocol will be documented in a protocol deviation form and filed in the study master file.
A NorCRIN SOP is in place describing the procedure for identifying non-compliances, escalation to the central team and assessment of whether a non-compliance /deviation may be a potential Serious Breach.

9. SERIOUS BREACHES

A "serious breach" is a breach of the protocol or of the conditions or principles of Good Clinical Practice which is likely to affect to a significant degree –

a) the safety or physical or mental integrity of the trial subjects; or
b) the scientific value of the research.

In the event that a serious breach is suspected the Sponsor must be contacted within one working day. In collaboration with the CI, the serious breach will be reviewed by the Sponsor and, if appropriate, the Sponsor will report it to the approving Norwegian Medicines Agency (NoMA) within seven calendar days.

10. ETHICAL AND REGULATORY CONSIDERATIONS

10.1 Declaration of Helsinki

The Investigators will ensure that this study is conducted in accordance with the principles of the Declaration of Helsinki.

10.2 Guidelines for Good Clinical Practice

The Investigators will ensure that this trial is conducted in accordance with relevant regulations and with Good Clinical Practice.

10.3 Approvals

Following Sponsor approval, the protocol, informed consent form, participant information sheets and any proposed informing material will be submitted to an appropriate Research Ethics Committee (REC) and regulatory authorities for written approval. The PI will ensure and confirm correct regulatory approvals are gained prior to recruitment.
The Investigator will submit and, where necessary, obtain approval from the above parties for all substantial amendments to the original approved documents.

10.4 Reporting

The CI shall submit once a year throughout the clinical trial, to NoMA. In addition, an End of Trial notification and final report will be submitted to NoMA.

10.5 Participant Confidentiality

The study will comply with the Norwegian General Data Protection Regulation (GDPR) and Data Protection Act 2018, which require data to be anonymised as soon as it is practical to do so. The processing of the personal data of participants will be minimised by making use of a unique participant study number only on all study documents and any electronic database(s).

A separate electronic file will be securely stored providing linkage between the unique participant identification numbers and the contact details. All documents will be stored securely and only accessible by study staff and authorised personnel. The study staff will safeguard the privacy of participants' personal data.

10.6 Expenses and Benefits

There will be no prescription charges for trial antiviral agents incurred by trial participants.

11. FINANCE AND INSURANCE

11.1 Funding

The study is funded by the Norwegian Ministry of Health (MoH) through the KlinBeForsk programme, funds from the Regional Health Authority of Western Norway, the Municipality of Bergen and the University of Bergen.
The MoH will provide the antiviral agents to be evaluated in the trial without cost to the trial budget for trial use.

11.2 Insurance

Patients are insured in accordance with the Product Liability Act in the Drug Insurance and the Patient Injuries Act.

11.3 Contractual arrangements

Appropriate contractual arrangements will be put in place with all third parties.

12. PUBLICATION POLICY

The Investigators (those listed on the protocol and others to be decided at publication) will be involved in reviewing drafts of the manuscripts, abstracts, press releases and any other publications arising from the study. Authors will acknowledge the study funders. Authorship will be determined in accordance with the ICMJE guidelines and other contributors will be acknowledged.

13. DEVELOPMENT OF A NEW PRODUCT/ PROCESS OR THE GENERATION OF INTELLECTUAL PROPERTY

Ownership of IP generated by employees of Helse Bergen and the University vests in the institutions. Helse Bergen and the University will ensure appropriate arrangements are in place as regards any new IP arising from the trial.

14. ARCHIVING

Archiving will be done according to the NorCRIN SOP and study specific working instructions. Research documents with personal information, such as consent forms, will be held securely at the University of Bergen's archiving facility according to the NorCRIN Archiving SOP.

15. REFERENCES

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16. APPENDIX A: SCHEDULE OF PROCEDURES

Procedures	**Day 0**	**Day 1**	**Day 2**	**Diary day 0-7, 14, 21 and 28, and 3 and 6 months**	**Day 0 – Up to 1 year**	**3 months**	**6 months**	**12 months**
	Eligibility, consent and baseline completed by participant and trial team[#]	**Telephone call: confirm pregnancy test**	**Telephone call to all participants**	**Symptom Diaries completed by participant online/ phone**	**Retrospective data collection by study team [$]**	**Exploratory substudies**	**Exploratory substudies**	**Exploratory substudies**
Informed consent	X							
Questionnaire				X				
Pregnancy test confirmation		X[£]						
Demographics	X							
Medical history	X				X			
Concomitant medications	X				X			
Eligibility assessment	X							
Randomisation	X							
Dispensing of trial drugs	X							
Compliance			X	X				
Primary endpoint and secondary outcomes				X	X			
Adverse event assessments			X	X				
Evidence of sequalae and health care utilization				X	X			
Blood samples exploratory substudy	X					X	X	X
Sputum sample exploratory substudy	X							
MRI						X	X	
EEG						X	X	

The trial team will retrospectively retrieve relevant information from Norwegian health registries, including emergency hospitalization events (Norwegian Patient Registry (NPR)), details concerning COVID-related hospital admittance (Norwegian Pandemic Registry), mortality and cause of death (Norwegian Cause of Death Registry), contacts with primary care (Norwegian Registry for Primary Health Care (KPR)), COVID vaccine history (Norwegian Immunisation Registry (Sysvak)), drug prescription (Norwegian Prescription Database (NorPD), Norwegian Surveillance System for Communicable Diseases (MSIS) and sick leave (The Sickness Absence Registry).

All patient-related procedures at Day 0 will occur after the informed consent form is signed.

Further pregnancy testing (home test) may be done during the course of the study should pregnancy be suspected

17. APPENDIX B: AMENDMENT HISTORY

Amendment No.	Protocol Version No.	Date issued	Author(s) of changes	Details of Changes made

Lists details of all protocol amendments whenever a new version of the protocol is produced.

Protocol amendments must be submitted to the Sponsor for approval prior to submission to the REC committee, HRA (where required) and/or MHRA.

18. APPENDIX C: SUPPLEMENTARY MATERIAL

A. Abbreviations

3CLpro	3C-like protease
ADR	Adaptive Design Report
AE	Adverse event
AR	Adverse reaction
AUC24	Area under the curve at 24 hours
BMI	Body Mass Index
CACE	CACE - Complier Average Causal Effect
CD4	Cluster of differentiation 4
CI	Chief Investigator
CRF	Case Report Form
CT	Clinical Trials
CTA	Clinical Trials Authorisation
CTU	Clinical Trials Unit
CYP3A	Cytochrome P450 3A4
DHSC	Department of Health and Social Care
DSMC	Data Monitoring Committee / Data and Safety Monitoring Committee
DSUR	Development Safety Update Report
eCFR	electronic Case Report Form
EDTA	Ethylenediaminetetraacetic acid
EEG	Electroencephalogram
ELISpot	Enzyme-linked immune absorbent spot
EMA	Emergency Medical Assistance
EPIC-HR	Evaluation of Protease Inhibition for Covid-19 in High-Risk Patients
fMRI	functional Magnetic Resonance Imaging
GCP	Good Clinical Practice
GDF-15	Growth differentiation factor 15
GDPR	General Data Protection Regulation
GP	General Practitioner
GPDPR	General Practice Data for planning and research
HCP	Healthcare professional
HMG Co-A	3-hydroxy-3-methylglutaryl coenzyme A
HRA	Health Research Authority
HUS	Haukeland University Hospital
IB	Investigators Brochure
ICF	Informed Consent Form
ICH	International Conference on Harmonization
ICMJE	International Committee of Medical Journal Editors
IGS	Department of Global Public Health and Primary Care, UiB
IMP	Investigational Medicinal Product
K2	Department of Clinical Science, UiB

KPR	Norwegian Registry for Primary Health Care
LAG-3	Lymphocyte-activation gene 3
LARC	Long-acting reversible contraceptive
mAb	monoclonal antibody treatment
MAdCAM	Mucosal addressin cell adhesion molecule
MHRA	Medicines and Healthcare products Regulatory Agency
mITT	modified intent-to-treat
MoH	Norwegian Ministry of Health
Mpro	SARS-CoV-2 main protease
MRI	Magnetic resonance imaging
M-SAP	Master Statistical Analysis Plan
MSIS	Norwegian Surveillance System for Communicable Diseases
NCAD	Neuronal cadherin
NHS	National Health Service
NNT	Numbers to treat
NoMA	Norwegian Medicines Agency
NorCRIN	Norwegian Clinical Research Infrastructures Network
NorPD	Norwegian Prescription Database
NPR	Norwegian Patient Registry
NTNU	Norwegian University of Science and Technology
PANORAMIC Norway	PAxlovid loNg cOvid-19 pRevention triAl with recruitMent In the Community in Norway
PCR	Polymerase chain reaction
PDE5	Phosphodiesterase type 5
PI	Principal Investigator
PIS	Participant/ Patient Information Sheet
PraksisNett	General Practice Data
PT	Core project team
QALY	Quality-adjusted life year
RCGP	Royal College of General Practitioners
RCT	Randomized controlled trial
REC	Research Ethics Committee
RSI	Reference Safety Information
SAC	Statistical Analysis Committee
SAE	Serious Adverse Event
SAR	Serious Adverse Reaction
SDV	Source Data Verification
SmPC	Summary of Medicinal Product Characteristics
SOP	Standard Operating Procedure

SUSAR	Suspected Unexpected Serious Adverse Reactions
Sysvak	Norwegian Immunisation Registry
TIM-3	T-cell immunoglobulin mucin-3
TSC	Trial Steering Committee
TMF	Trial Master File
TMG	Trial Management Group
UiB	University of Bergen

B. Key Trial Contacts

Chief Investigator	Professor Nina Langeland E mail: Nina.langeland@uib.no Mobile: +47 416 16 450
Sponsor	Department of Medicine Helse Bergen HF Jonas Lies Vei 87 N5021 Bergen, Norway
Funder(s)	KlinBeForsk programme, Regional Health Authority of Western Norway Municipality of Bergen University of Bergen
Statistician	Professor Rolv Terje Lie E mail: rolv.lie@uib.no Mobile: +47 930 87 160
Committees	**DSMC Chair:** Bjørn Tore Gjertsen, Haukeland University Hospital **DSMC Members:** Knut Engedal, University of Oslo
	TSC Chair Pål Aukrust, Oslo University Hospital **TSC Members** Axel Sandvig, NTNU Maja Wilhelmsen, UNN Rolv Terje Lie, UiB Tuva Børresdatter Dahl, OUD Nina Langeland, HUS/UiB **PPI representatives** TBC

C. Adverse Events
Definitions

Adverse Event (AE)	Any untoward medical occurrence in a participant to whom a medicinal product has been administered, including occurrences which are not necessarily caused by or related to that product.
Adverse Reaction (AR)	An untoward and unintended response in a participant to an investigational medicinal product which is related to any dose administered to that participant. The phrase "response to an investigational medicinal product" means that a causal relationship between a trial medication and an AE is at least a reasonable possibility, i.e. the relationship cannot be ruled out. All cases judged by either the reporting medically qualified professional or the Sponsor as having a reasonable suspected causal relationship to the trial medication qualify as adverse reactions.
Serious Adverse Event (SAE)	A serious adverse event is any untoward medical occurrence that: • results in death • is life-threatening • requires inpatient hospitalisation or prolongation of existing hospitalisation • results in persistent or significant disability/incapacity • consists of a congenital anomaly or birth defect*. Other 'important medical events' may also be considered a serious adverse event when, based upon appropriate medical judgement, the event may jeopardise the participant and may require medical or surgical intervention to prevent one of the outcomes listed above. NOTE: The term "life-threatening" in the definition of "serious" refers to an event in which the participant was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe. *NOTE: Pregnancy is not, in itself an SAE. In the event that a participant or their partner becomes pregnant whilst taking part in a clinical trial or during a stage where the foetus could have been exposed to the medicinal product (in the case of the active substance or one of its metabolites having a long half-life) the pregnancy should be followed up by the investigator until delivery for congenital abnormality or birth defect, at which point it would fall within the definition of "serious".
Serious Adverse Reaction (SAR)	An adverse event that is both serious and, in the opinion of the reporting Investigator, believed with reasonable probability to be due to one of the trial antiviral agents, based on the information provided.

Suspected Unexpected Serious Adverse Reaction (SUSAR)	A serious adverse reaction, the nature and severity of which is not consistent with the Reference Safety Information for the medicinal product in question set out: • in the case of a product with a marketing authorisation, in the approved summary of product characteristics (SmPC) for that product • in the case of any other investigational medicinal product, in the approved investigator's

NB: To avoid confusion or misunderstanding the difference between the terms "serious" and "severe", the following note of clarification is provided: "Severe" is often used to describe intensity of a specific event, which may be of relatively minor medical significance.

19. APPENDIX D: CASE REPORT FORMS

Covid-19 infeksjon: Panoramic Norway dag 0

Dato i dag: _____/_____/_____

Pasient ID _____

1. **Etter du testet positiv, har du nå plager som du ikke hadde før Covid-19?**

☐ Feber
☐ Tung pust
☐ Prikking/nummenhet i armer/ben/kropp
☐ Hodepine
☐ Svimmelhet
☐ Hjertebank
☐ Kvalme
☐ Oppkast
☐ Diare
☐ Magesmerter
☐ Redusert lukte/smakssans
☐ Sliten
☐ Søvnproblemer
☐ Redusert hukommelse
☐ Konsentrasjonsproblemer
☐ Brystsmerter
☐ Muskel eller leddsmerter
☐ Deprimert/nedfor
☐ Andre symptomer, nevn hvilke: _____
☐ Nei, ingen symptomer

2. **Har du noen kroniske sykdommer?** ☐ Nei ☐ Ja

→ Hvis ja, hvilke sykdommer:

☐ Diabetes
☐ Astma eller KOLS
☐ Medfødte sykdommer slik som Down's sykdom
☐ Hjertesykdom eller høyt blodtrykk
☐ Hjernesykdom (slag, demens, epilepsi)
☐ Revmatisk sykdom
☐ Annen kronisk sykdom. Vennligst spesifiser: _____

3. **Bruker du noen faste medisiner?** ☐ Nei ☐ Ja

→ Navn på medisin (nevn alle): _____

4. **Høyde**: _____ cm **Vekt:** ____ kg

5. **Har du tidligere testet positiv for Covid-19?** ☐ Nei ☐ Ja

→ Hvis ja, hvor mange ganger? _____

→ Dato eller måned og år siste gang du testet positiv _____

6. **Har du tatt Covid-19 vaksine?** ☐ Nei ☐ Ja

→ Hvis ja, hvor mange doser? _____

→ Når var siste dose? _____

7. **Hva var din yrkessituasjon før du fikk covid denne gangen?**

☐ I jobb ☐ Student ☐ Sykmeldt ☐ Arbeidsledig ☐ Ufør
☐ Pensjonist

8. **Hvor mange bor i husstanden inkludert deg:**

Antall barn under 18: _____

Antall voksne: _____

9. **Har du tidligere gjennomført MR av hodet?** ☐ Nei ☐ Ja

Covid-19 infeksjon: Panoramic Norway dag 1

Pasient ID _____ **Dato i dag:** ___/____

1. **Tok du alle studiemedisinene i går?** ☐ Nei ☐ Ja

→ Hvis nei, hvor mange tabletter tok du? _____

2. **Har du symptomer i dag?**

☐ Feber
☐ Tung pust
☐ Prikking/nummenhet i armer/ben/kropp
☐ Hodepine
☐ Svimmelhet
☐ Hjertebank
☐ Kvalme
☐ Oppkast
☐ Diare
☐ Magesmerter
☐ Redusert lukte/smakssans
☐ Mer sliten
☐ Søvnproblemer
☐ Redusert hukommelse
☐ Konsentrasjonsproblemer
☐ Brystsmerter
☐ Hoste
☐ Utslett
☐ Muskel eller leddsmerter
☐ Deprimert/nedfor
☐ Andre symptomer, nevn hvilke: _____
☐ Nei, ingen symptomer

3. **Har du vært innlagt sykehus?** ☐ Nei ☐ Ja

4. **Har du vært i kontakt med fastlege eller legevakt på grunn av covid?** ☐ Nei ☐ Ja

5. **(Spm. til kvinner) Hvis du fikk graviditetstest hos oss i går, var den positiv?** ☐ Nei ☐ Ja

Covid-19 infeksjon: Panoramic Norway dag 2

Pasient ID: _____ **Dato i dag:** ___/___/___

1. **Tok du alle studiemedisinene i går?** ☐ Nei ☐ Ja

→ Hvis nei, hvor mange tabletter tok du? _____

2. **Har du symptomer i dag?**

☐ Feber
☐ Tung pust
☐ Prikking/nummenhet i armer/ben/kropp
☐ Hodepine
☐ Svimmelhet
☐ Hjertebank
☐ Kvalme
☐ Oppkast
☐ Diare
☐ Magesmerter
☐ Redusert lukte/smakssans
☐ Mer sliten
☐ Søvnproblemer
☐ Redusert hukommelse
☐ Konsentrasjonsproblemer
☐ Brystsmerter
☐ Hoste
☐ Utslett
☐ Muskel eller leddsmerter
☐ Deprimert/nedfor
☐ Andre symptomer, nevn hvilke: _____
☐ Nei, ingen symptomer

3. **Har du vært innlagt sykehus?** ☐ Nei ☐ Ja

4. **Har du vært i kontakt med fastlege eller legevakt på grunn av covid?** ☐ Nei ☐ Ja

Covid-19 infeksjon: Panoramic Norway dag 3

Pasient ID: _____ **Dato i dag:** ___/___/___

1. Tok du alle studiemedisinene i går? ☐ Nei ☐ Ja

→ Hvis nei, hvor mange tabletter tok du? _____

2. Har du symptomer i dag?

☐ Feber
☐ Tung pust
☐ Prikking/nummenhet i armer/ben/kropp
☐ Hodepine
☐ Svimmelhet
☐ Hjertebank
☐ Kvalme
☐ Oppkast
☐ Diare
☐ Magesmerter
☐ Redusert lukte/smakssans
☐ Mer sliten
☐ Søvnproblemer
☐ Redusert hukommelse
☐ Konsentrasjonsproblemer
☐ Brystsmerter
☐ Hoste
☐ Utslett
☐ Muskel eller leddsmerter
☐ Deprimert/nedfor
☐ Andre symptomer, nevn hvilke: _____
☐ Nei, ingen symptomer

3. Har du vært innlagt sykehus? ☐ Nei ☐ Ja

4. Har du vært i kontakt med fastlege eller legevakt på grunn av covid? ☐ Nei ☐ Ja

Covid-19 infeksjon: Panoramic Norway dag 4

Pasient ID: _____ **Dato i dag:** __/__/____

1. Tok du alle studiemedisinene i går? ☐ Nei ☐ Ja

→ Hvis nei, hvor mange tabletter tok du? _____

2. Har du symptomer i dag?

☐ Feber
☐ Tung pust
☐ Prikking/nummenhet i armer/ben/kropp
☐ Hodepine
☐ Svimmelhet
☐ Hjertebank
☐ Kvalme
☐ Oppkast
☐ Diare
☐ Magesmerter
☐ Redusert lukte/smakssans
☐ Mer sliten
☐ Søvnproblemer
☐ Redusert hukommelse
☐ Konsentrasjonsproblemer
☐ Brystsmerter
☐ Hoste
☐ Utslett
☐ Muskel eller leddsmerter
☐ Deprimert/nedfor
☐ Andre symptomer, nevn hvilke: _____
☐ Nei, ingen symptomer

3. Har du vært innlagt sykehus? ☐ Nei ☐ Ja

4. Har du vært i kontakt med fastlege eller legevakt på grunn av covid? ☐ Nei ☐ Ja

Covid-19 infeksjon: Panoramic Norway dag 5

Pasient ID: _____ **Dato i dag:** ___/___/____

1. Tok du alle studiemedisinene i går? ☐ Nei ☐ Ja

→ Hvis nei, hvor mange tabletter tok du? _____

2. Har du symptomer i dag?

☐ Feber
☐ Tung pust
☐ Prikking/nummenhet i armer/ben/kropp
☐ Hodepine
☐ Svimmelhet
☐ Hjertebank
☐ Kvalme
☐ Oppkast
☐ Diare
☐ Magesmerter
☐ Redusert lukte/smakssans
☐ Mer sliten
☐ Søvnproblemer
☐ Redusert hukommelse
☐ Konsentrasjonsproblemer
☐ Brystsmerter
☐ Hoste
☐ Utslett
☐ Muskel eller leddsmerter
☐ Deprimert/nedfor
☐ Andre symptomer, nevn hvilke: _____
☐ Nei, ingen symptomer

3. Har du vært innlagt sykehus? ☐ Nei ☐ Ja

4. Har du vært i kontakt med fastlege eller legevakt på grunn av covid? ☐ Nei ☐ Ja

Covid-19 infeksjon: Panoramic Norway dag 6

Pasient ID: _____ **Dato i dag:** ___/___/____

1. **Tok du alle studiemedisinene i går?** ☐ Nei ☐ Ja

→ Hvis nei, hvor mange tabletter tok du? _____

2. **Har du symptomer i dag?**

☐ Feber
☐ Tung pust
☐ Prikking/nummenhet i armer/ben/kropp
☐ Hodepine
☐ Svimmelhet
☐ Hjertebank
☐ Kvalme
☐ Oppkast
☐ Diare
☐ Magesmerter
☐ Redusert lukte/smakssans
☐ Mer sliten
☐ Søvnproblemer
☐ Redusert hukommelse
☐ Konsentrasjonsproblemer
☐ Brystsmerter
☐ Hoste
☐ Utslett
☐ Muskel eller leddsmerter
☐ Deprimert/nedfor
☐ Andre symptomer, nevn hvilke: _____
☐ Nei, ingen symptomer

3. **Har du vært innlagt sykehus?** ☐ Nei ☐ Ja

4. **Har du vært i kontakt med fastlege eller legevakt på grunn av covid?** ☐ Nei ☐ Ja

Covid-19 infeksjon: Panoramic Norway dag 7

Pasient ID: _____ **Dato i dag:** ___/___/____

1. Har du symptomer i dag?

☐ Feber
☐ Tung pust
☐ Prikking/nummenhet i armer/ben/kropp
☐ Hodepine
☐ Svimmelhet
☐ Hjertebank
☐ Kvalme
☐ Oppkast
☐ Diare
☐ Magesmerter
☐ Redusert lukte/smakssans
☐ Mer sliten
☐ Søvnproblemer
☐ Redusert hukommelse
☐ Konsentrasjonsproblemer
☐ Brystsmerter
☐ Hoste
☐ Utslett
☐ Muskel eller leddsmerter
☐ Deprimert/nedfor
☐ Andre symptomer, nevn hvilke: _____
☐ Nei, ingen symptomer

2. Har du vært innlagt sykehus? ☐ Nei ☐ Ja

3. Har du vært i kontakt med fastlege eller legevakt på grunn av covid? ☐ Nei ☐ Ja

Covid-19 infeksjon: Panoramic Norway Uke 2

Pasient ID: _____ **Dato i dag:** ___/___/____

1. Etter du testet positiv, har du nå plager som du ikke hadde før Covid-19?

☐ Feber
☐ Tung pust
☐ Prikking/nummenhet i armer/ben/kropp
☐ Hodepine
☐ Svimmelhet
☐ Hjertebank
☐ Kvalme
☐ Hoste
☐ Andre plager, nevn hvilke: _____
☐ Nei, ingen plager

☐ Magesmerter
☐ Oppkast
☐ Diarre
☐ Redusert lukte/smakssans
☐ Søvnproblemer
☐ Brystsmerter
☐ Muskel eller leddsmerter

Spørsmålene nedenfor gjelder symptomer nå:

2. Har du problemer med at du føler deg sliten?

☐ Mindre enn vanlig ☐ Ikke mer enn vanlig ☐ Mer enn vanlig
☐ Mye mer enn vanlig

3. Har du vansker med å konsentrere deg?

☐ Mindre enn vanlig ☐ Som vanlig ☐ Mer enn vanlig
☐ Mye mer enn vanlig

4. Hvordan er hukommelsen din?

☐ Bedre enn vanlig ☐ Ikke verre enn vanlig ☐ Verre enn vanlig
☐ Mye verre enn vanlig

5. Hvis du har dårlig hukommelse, konsentrasjonsvansker eller er sliten for tiden, omtrent hvor mye av tiden?

☐ 25 % av tiden ☐ 50 % av tiden ☐ 75 % av tiden
☐ Hele tiden

6. Hvis du for tiden har dårlig hukommelse, konsentrasjonsvansker eller er sliten, omtrent hvor lenge har det vart?

☐ < 1 uke ☐ < 3 måneder ☐ 3-6 måneder
☐ 6 måneder eller mer

7. Har du følt deg nedfor og deprimert?

☐ Mindre enn vanlig ☐ Ikke mer enn vanlig ☐ Mer enn vanlig

☐ Mye mer enn vanlig

8. Er du tungpustet?

☐ Mindre enn vanlig ☐ Ikke mer enn vanlig ☐ Mer enn vanlig

☐ Mye mer enn vanlig

9. Har du vært innlagt sykehus? ☐ Nei ☐ Ja

10. Har du vært i kontakt med fastlege eller legevakt på grunn av covid? ☐ Nei ☐ Ja

→ Hvis ja, hvor mange ganger: _____

11. Hvor mange andre i familien har blitt smittet?

Antall barn under 18: _____
Antall voksne: _____

12. Har du vært borte fra jobb eller studie/skole på grunn av covid? ☐ Nei ☐ Ja

→ Hvis ja, hvor mange dager: _____

13. Var andre voksne i familien borte fra jobb på grunn av covid? ☐ Nei ☐ Ja

→ Hvis ja, hvor mange dager: _____

14. Har du eller partneren din blitt gravid siden du ble med i studien? ☐ Nei ☐ Ja

EQ-5D-5L validert skjema

Under hver overskrift ber vi deg krysse av den ENE boksen som best beskriver helsen din I DAG.

GANGE

☐ Jeg har ingen problemer med å gå omkring

☐ Jeg har litt problemer med å gå omkring

☐ Jeg har middels store problemer med å gå omkring

☐ Jeg har store problemer med å gå omkring

☐ Jeg er ute av stand til å gå omkring

PERSONLIG STELL

☐ Jeg har ingen problemer med å vaske meg eller kle meg

☐ Jeg har litt problemer med vaske meg eller kle meg

☐ Jeg har middels store problemer med å vaske meg eller kle meg

☐ Jeg har store problemer med å vaske meg eller kle meg

☐ Jeg er ute av stand til å vaske meg eller kle meg

VANLIGE GJØREMÅL *(f. eks. arbeid, studier, husarbeid, familie- eller fritidsaktiviteter)*

☐ Jeg har ingen problemer med å utføre mine vanlige gjøremål

☐ Jeg har litt problemer med å utføre mine vanlige gjøremål

☐ Jeg har middels store problemer med å utføre mine vanlige gjøremål

☐ Jeg har store problemer med å utføre mine vanlige gjøremål

☐ Jeg er ute av stand til å utføre mine vanlige gjøremål

SMERTER/UBEHAG

☐ Jeg har verken smerter eller ubehag

☐ Jeg har litt smerter eller ubehag

☐ Jeg har middels sterke smerter eller ubehag

☐ Jeg har sterke smerter eller ubehag

☐ Jeg har svært sterke smerter eller ubehag

ANGST/DEPRESJON

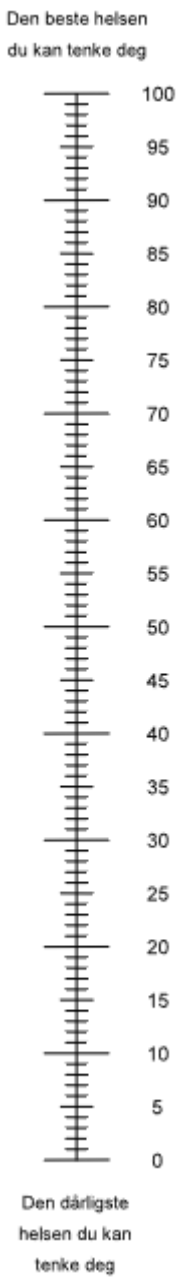
☐ Jeg er verken engstelig eller deprimert

☐ Jeg er litt engstelig eller deprimert

☐ Jeg er middels engstelig eller deprimert

☐ Jeg er svært engstelig eller deprimert

☐ Jeg er ekstremt engstelig eller deprimert



· Vi vil gjerne vite hvor god eller dårlig helsen din er I DAG.

· Denne skalaen er nummerert fra 0 til 100.

· 100 betyr den beste helsen du kan tenke deg. 0 betyr den dårligste helsen du kan tenke deg.

· Sett en X på skalaen for å angi hvordan helsen din er I DAG.

· Skriv deretter tallet du merket av på skalaen
inn i boksen nedenfor.

Helsen din i dag: _____

Covid-19 infeksjon: Panoramic Norway Uke 3

Pasient ID: _____ **Dato i dag:** ___/___/____

1. Etter du testet positiv, har du nå plager som du ikke hadde før Covid-19?

☐ Feber
☐ Tung pust
☐ Prikking/nummenhet i armer/ben/kropp
☐ Hodepine
☐ Svimmelhet
☐ Hjertebank
☐ Kvalme
☐ Hoste
☐ Andre plager, nevn hvilke: _____
☐ Nei, ingen plager

☐ Magesmerter
☐ Oppkast
☐ Diarre
☐ Redusert lukte/smakssans
☐ Søvnproblemer
☐ Brystsmerter
☐ Muskel eller leddsmerter

2. Har du vært innlagt sykehus? ☐ Nei ☐ Ja

3. Har du vært i kontakt med fastlege eller legevakt på grunn av covid? ☐ Nei ☐ Ja

→ Hvis ja, hvor mange ganger: _____

4. Hvor mange andre i familien enn deg har blitt smittet?

Antall barn under 18: _____
Antall voksne: _____

5. Har du vært borte fra jobb eller studie/skole på grunn av covid? ☐ Nei ☐ Ja

→ Hvis ja, hvor mange dager: _____

6. Var andre voksne i familien borte fra jobb? ☐ Nei ☐ Ja

→ Hvis ja, hvor mange dager: _____

Covid-19 infeksjon: Panoramic Norway Uke 4

Pasient ID: _____ **Dato i dag:** ___/___/____

1. Etter du testet positiv, har du nå plager som du ikke hadde før Covid-19?

☐ Feber
☐ Tung pust
☐ Prikking/nummenhet i armer/ben/kropp
☐ Hodepine
☐ Svimmelhet
☐ Hjertebank
☐ Kvalme
☐ Hoste
☐ Andre plager, nevn hvilke: _____
☐ Nei, ingen plager

☐ Magesmerter
☐ Oppkast
☐ Diarre
☐ Redusert lukte/smakssans
☐ Søvnproblemer
☐ Brystsmerter
☐ Muskel eller leddsmerter

Spørsmålene nedenfor gjelder symptomer nå:

2. Har du problemer med at du føler deg sliten?

☐ Mindre enn vanlig ☐ Ikke mer enn vanlig ☐ Mer enn vanlig
☐ Mye mer enn vanlig

3. Har du vansker med å konsentrere deg?

☐ Mindre enn vanlig ☐ Som vanlig ☐ Mer enn vanlig
☐ Mye mer enn vanlig

4. Hvordan er hukommelsen din?

☐ Bedre enn vanlig ☐ Ikke verre enn vanlig ☐ Verre enn vanlig
☐ Mye verre enn vanlig

5. Hvis du har dårlig hukommelse, konsentrasjonsvansker eller er sliten for tiden, omtrent hvor mye av tiden?

☐ 25 % av tiden ☐ 50 % av tiden ☐ 75 % av tiden
☐ Hele tiden

6. Hvis du for tiden har dårlig hukommelse, konsentrasjonsvansker eller er sliten, omtrent hvor lenge har det vart?

☐ < 1 uke ☐ < 3 måneder ☐ 3-6 måneder

☐ 6 måneder eller mer

7. Har du følt deg nedfor og deprimert?

☐ Mindre enn vanlig ☐ Ikke mer enn vanlig ☐ Mer enn vanlig

☐ Mye mer enn vanlig

8. Er du tungpustet?

☐ Mindre enn vanlig ☐ Ikke mer enn vanlig ☐ Mer enn vanlig

☐ Mye mer enn vanlig

9. Har du vært innlagt sykehus? ☐ Nei ☐ Ja

10. Har du vært i kontakt med fastlege eller legevakt på grunn av covid? ☐ Nei ☐ Ja

→ Hvis ja, hvor mange ganger: _____

11. Hvor mange andre i familien enn deg har blitt smittet?

Antall barn under 18: _____
Antall voksne: _____

12. Har du eller partneren din blitt gravid siden du ble med i studien? ☐ Nei ☐ Ja

13. Var du borte fra jobb på grunn av covid? ☐ Nei ☐ Ja

→ Hvis ja, hvor mange dager:

100% fravær - antall dager _____
75-95% fravær - antall dager _____
50-70% fravær - antall dager _____
30-45% fravær - antall dager _____
20% fravær - antall dager _____

14. Var andre voksne i familien din borte fra jobb? ☐ Nei ☐ Ja

→ Hvis ja, hvor mange dager: _____

EQ-5D-5L validert skjema

Under hver overskrift ber vi deg krysse av den ENE boksen som best beskriver helsen din I DAG.

GANGE

☐ Jeg har ingen problemer med å gå omkring

☐ Jeg har litt problemer med å gå omkring

☐ Jeg har middels store problemer med å gå omkring

☐ Jeg har store problemer med å gå omkring

☐ Jeg er ute av stand til å gå omkring

PERSONLIG STELL

☐ Jeg har ingen problemer med å vaske meg eller kle meg

☐ Jeg har litt problemer med vaske meg eller kle meg

☐ Jeg har middels store problemer med å vaske meg eller kle meg

☐ Jeg har store problemer med å vaske meg eller kle meg

☐ Jeg er ute av stand til å vaske meg eller kle meg

VANLIGE GJØREMÅL *(f. eks. arbeid, studier, husarbeid, familie- eller fritidsaktiviteter)*

☐ Jeg har ingen problemer med å utføre mine vanlige gjøremål

☐ Jeg har litt problemer med å utføre mine vanlige gjøremål

☐ Jeg har middels store problemer med å utføre mine vanlige gjøremål

☐ Jeg har store problemer med å utføre mine vanlige gjøremål

☐ Jeg er ute av stand til å utføre mine vanlige gjøremål

SMERTER/UBEHAG

☐ Jeg har verken smerter eller ubehag

☐ Jeg har litt smerter eller ubehag

☐ Jeg har middels sterke smerter eller ubehag

☐ Jeg har sterke smerter eller ubehag

☐ Jeg har svært sterke smerter eller ubehag

ANGST/DEPRESJON

☐ Jeg er verken engstelig eller deprimert

☐ Jeg er litt engstelig eller deprimert

☐ Jeg er middels engstelig eller deprimert

☐ Jeg er svært engstelig eller deprimert

☐ Jeg er ekstremt engstelig eller deprimert

· Vi vil gjerne vite hvor god eller dårlig helsen din er I DAG.

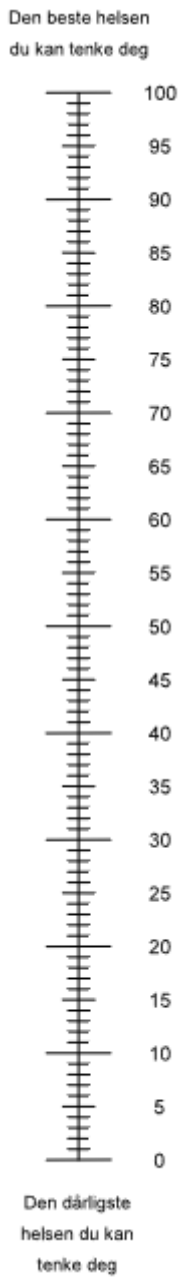
· Denne skalaen er nummerert fra 0 til 100.

· 100 betyr den beste helsen du kan tenke deg. 0 betyr den dårligste helsen du kan tenke deg.

· Sett en X på skalaen for å angi hvordan helsen din er I DAG.

· Skriv deretter tallet du merket av på skalaen
inn i boksen nedenfor.

Helsen din i dag: _____



Covid-19 infeksjon: Panoramic Norway 3 mnd oppfølging

Pasient ID: _____ **Dato i dag:** ___/___/____

1. **Etter du testet positiv, har du nå plager som du ikke hadde før Covid-19?** ☐ Nei ☐ Ja

→ Hvis ja, hvilke symptomer (vennligst kryss av):

☐ Feber
☐ Tung pust
☐ Prikking/nummenhet i armer/ben/kropp
☐ Hodepine
☐ Svimmelhet
☐ Hjertebank
☐ Hoste
☐ Redusert lukte/smakssans
☐ Søvnproblemer
☐ Brystsmerter
☐ Muskel eller leddsmerter
☐ Kvalme
☐ Oppkast
☐ Diarre

Andre symptomer: _____

2. **Har du blitt covid-smittet på nytt?** ☐ Nei ☐ Ja

→ Hvis ja, når: _____

Spørsmålene nedenfor gjelder symptomer nå:

3. **Har du problemer med at du føler deg sliten?**
   ☐ Mindre enn vanlig ☐ Ikke mer enn vanlig ☐ Mer enn vanlig
   ☐ Mye mer enn vanlig
4. **Har du vansker med å konsentrere deg?**
   ☐ Mindre enn vanlig ☐ Som vanlig ☐ Mer enn vanlig
   ☐ Mye mer enn vanlig
5. **Hvordan er hukommelsen din?**
   ☐ Bedre enn vanlig ☐ Ikke verre enn vanlig ☐ Verre enn vanlig
   ☐ Mye verre enn vanlig
6. **Hvis du har dårlig hukommelse, konsentrasjonsvansker eller er sliten for tiden, omtrent hvor mye av tiden?**
   ☐ 25 % av tiden ☐ 50 % av tiden ☐ 75 % av tiden
   ☐ Hele tiden

7. Hvis du for tiden har dårlig hukommelse, konsentrasjonsvansker eller er sliten, omtrent hvor lenge har det vart?

☐ < 1 uke ☐ < 3 måneder ☐ 3-6 måneder

☐ 6 måneder eller mer

8. Har du følt deg nedfor og deprimert?

☐ Mindre enn vanlig ☐ Ikke mer enn vanlig ☐ Mer enn vanlig

☐ Mye mer enn vanlig

9. Er du tungpustet?

☐ Mindre enn vanlig ☐ Ikke mer enn vanlig ☐ Mer enn vanlig

☐ Mye mer enn vanlig

10. Har du vært innlagt sykehus? ☐ Nei ☐ Ja

→ Hva var grunnen?: _____

11. Har du vært i kontakt med fastlege eller legevakt på grunn av covid? ☐ Nei ☐ Ja

→ Hvis ja, hvor mange ganger: _____

12. Har du eller partneren din blitt gravid siden du ble med i studien? ☐ Nei ☐ Ja

13. Var du borte fra jobb på grunn av covid? ☐ Nei ☐ Ja

→ Hvis ja, hvor mange dager:
100% fravær - antall dager _____
75-95% fravær - antall dager _____
50-70% fravær - antall dager _____
30-45% fravær - antall dager _____
20% fravær - antall dager _____

14. Var andre voksne i familien din borte fra jobb? ☐ Nei ☐ Ja

→ Hvis ja, hvor mange dager: _____

EQ-5D-5L validert skjema

Under hver overskrift ber vi deg krysse av den ENE boksen som best beskriver helsen din I DAG.

GANGE

☐ Jeg har ingen problemer med å gå omkring

☐ Jeg har litt problemer med å gå omkring

☐ Jeg har middels store problemer med å gå omkring

☐ Jeg har store problemer med å gå omkring

☐ Jeg er ute av stand til å gå omkring

PERSONLIG STELL

☐ Jeg har ingen problemer med å vaske meg eller kle meg

☐ Jeg har litt problemer med vaske meg eller kle meg

☐ Jeg har middels store problemer med å vaske meg eller kle meg

☐ Jeg har store problemer med å vaske meg eller kle meg

☐ Jeg er ute av stand til å vaske meg eller kle meg

VANLIGE GJØREMÅL *(f. eks. arbeid, studier, husarbeid, familie- eller fritidsaktiviteter)*

☐ Jeg har ingen problemer med å utføre mine vanlige gjøremål

☐ Jeg har litt problemer med å utføre mine vanlige gjøremål

☐ Jeg har middels store problemer med å utføre mine vanlige gjøremål

☐ Jeg har store problemer med å utføre mine vanlige gjøremål

☐ Jeg er ute av stand til å utføre mine vanlige gjøremål

SMERTER/UBEHAG

☐ Jeg har verken smerter eller ubehag

☐ Jeg har litt smerter eller ubehag

☐ Jeg har middels sterke smerter eller ubehag

☐ Jeg har sterke smerter eller ubehag

☐ Jeg har svært sterke smerter eller ubehag

ANGST/DEPRESJON

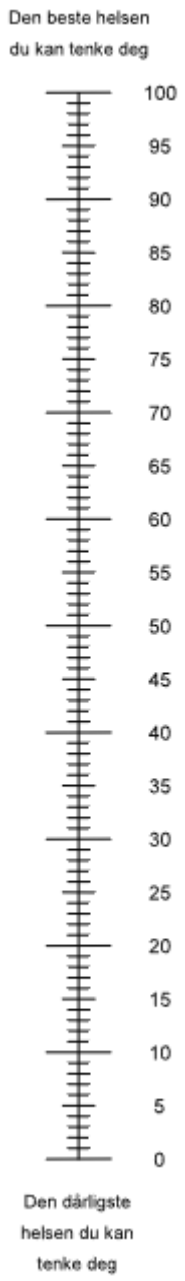
☐ Jeg er verken engstelig eller deprimert

☐ Jeg er litt engstelig eller deprimert

☐ Jeg er middels engstelig eller deprimert

☐ Jeg er svært engstelig eller deprimert

☐ Jeg er ekstremt engstelig eller deprimert



· Vi vil gjerne vite hvor god eller dårlig helsen din er I DAG.

· Denne skalaen er nummerert fra 0 til 100.

· 100 betyr den beste helsen du kan tenke deg. 0 betyr den dårligste helsen du kan tenke deg.

· Sett en X på skalaen for å angi hvordan helsen din er I DAG.

· Skriv deretter tallet du merket av på skalaen
inn i boksen nedenfor.

Helsen din i dag: _____

Covid-19 infeksjon: Panoramic Norway 6 mnd oppfølgning

Pasient ID: _____ **Dato i dag:** ___/___/____

1. **Etter du testet positiv, har du nå plager som du ikke hadde før Covid-19?** ☐ Nei ☐ Ja

→ Hvis ja, hvilke symptomer (vennligst kryss av):

☐ Feber
☐ Tung pust
☐ Prikking/nummenhet i armer/ben/kropp
☐ Hodepine
☐ Svimmelhet
☐ Hjertebank
☐ Hoste
☐ Redusert lukte/smakssans
☐ Søvnproblemer
☐ Brystsmerter
☐ Muskel eller leddsmerter
☐ Kvalme
☐ Oppkast
☐ Diarre

Andre symptomer: _____

2. **Har du blitt covid-smittet på nytt?** ☐ Nei ☐ Ja

→ Hvis ja, når: _____

Spørsmålene nedenfor gjelder symptomer nå:

3. **Har du problemer med at du føler deg sliten?**
   ☐ Mindre enn vanlig ☐ Ikke mer enn vanlig ☐ Mer enn vanlig
   ☐ Mye mer enn vanlig
4. **Har du vansker med å konsentrere deg?**
   ☐ Mindre enn vanlig ☐ Som vanlig ☐ Mer enn vanlig
   ☐ Mye mer enn vanlig
5. **Hvordan er hukommelsen din?**
   ☐ Bedre enn vanlig ☐ Ikke verre enn vanlig ☐ Verre enn vanlig
   ☐ Mye verre enn vanlig
6. **Hvis du har dårlig hukommelse, konsentrasjonsvansker eller er sliten for tiden, omtrent hvor mye av tiden?**
   ☐ 25 % av tiden ☐ 50 % av tiden ☐ 75 % av tiden
   ☐ Hele tiden

7. Hvis du for tiden har dårlig hukommelse, konsentrasjonsvansker eller er sliten, omtrent hvor lenge har det vart?

☐ < 1 uke ☐ < 3 måneder ☐ 3-6 måneder

☐ 6 måneder eller mer

8. Har du følt deg nedfor og deprimert?

☐ Mindre enn vanlig ☐ Ikke mer enn vanlig ☐ Mer enn vanlig

☐ Mye mer enn vanlig

9. Er du tungpustet?

☐ Mindre enn vanlig ☐ Ikke mer enn vanlig ☐ Mer enn vanlig

☐ Mye mer enn vanlig

10. Har du vært innlagt sykehus? ☐ Nei ☐ Ja

Hva var grunnen?: _____

11. Har du vært i kontakt med fastlege eller legevakt på grunn av covid? ☐ Nei ☐ Ja

→ Hvis ja, hvor mange ganger: _____

12. Har du eller partneren din blitt gravid siden du ble med i studien? ☐ Nei ☐ Ja

13. Var du borte fra jobb på grunn av covid? ☐ Nei ☐ Ja

→ Hvis ja, hvor mange dager:
100% fravær - antall dager _____
75-95% fravær - antall dager _____
50-70% fravær - antall dager _____
30-45% fravær - antall dager _____
20% fravær - antall dager _____

14. Var andre voksne i familien din borte fra jobb? ☐ Nei ☐ Ja

→ Hvis ja, hvor mange dager: _____

EQ-5D-5L validert skjema

Under hver overskrift ber vi deg krysse av den ENE boksen som best beskriver helsen din I DAG.

GANGE

☐ Jeg har ingen problemer med å gå omkring

☐ Jeg har litt problemer med å gå omkring

☐ Jeg har middels store problemer med å gå omkring

☐ Jeg har store problemer med å gå omkring

☐ Jeg er ute av stand til å gå omkring

PERSONLIG STELL

☐ Jeg har ingen problemer med å vaske meg eller kle meg

☐ Jeg har litt problemer med vaske meg eller kle meg

☐ Jeg har middels store problemer med å vaske meg eller kle meg

☐ Jeg har store problemer med å vaske meg eller kle meg

☐ Jeg er ute av stand til å vaske meg eller kle meg

VANLIGE GJØREMÅL *(f. eks. arbeid, studier, husarbeid, familie- eller fritidsaktiviteter)*

☐ Jeg har ingen problemer med å utføre mine vanlige gjøremål

☐ Jeg har litt problemer med å utføre mine vanlige gjøremål

☐ Jeg har middels store problemer med å utføre mine vanlige gjøremål

☐ Jeg har store problemer med å utføre mine vanlige gjøremål

☐ Jeg er ute av stand til å utføre mine vanlige gjøremål

SMERTER/UBEHAG

☐ Jeg har verken smerter eller ubehag

☐ Jeg har litt smerter eller ubehag

☐ Jeg har middels sterke smerter eller ubehag

☐ Jeg har sterke smerter eller ubehag

☐ Jeg har svært sterke smerter eller ubehag

ANGST/DEPRESJON

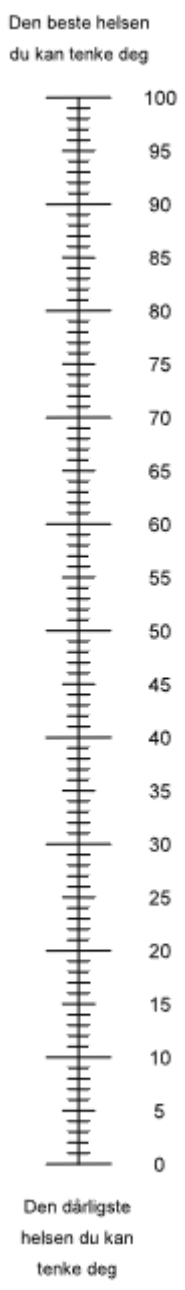
☐ Jeg er verken engstelig eller deprimert

☐ Jeg er litt engstelig eller deprimert

☐ Jeg er middels engstelig eller deprimert

☐ Jeg er svært engstelig eller deprimert

☐ Jeg er ekstremt engstelig eller deprimert



· Vi vil gjerne vite hvor god eller dårlig helsen din er I DAG.

· Denne skalaen er nummerert fra 0 til 100.

· 100 betyr den beste helsen du kan tenke deg. 0 betyr den dårligste helsen du kan tenke deg.

· Sett en X på skalaen for å angi hvordan helsen din er I DAG.

· Skriv deretter tallet du merket av på skalaen
inn i boksen nedenfor.

Helsen din i dag: _____

Covid-19 infeksjon: Panoramic Norway 12 mnd oppfølgning

Pasient ID: _____ **Dato i dag:** ___/___/____

1. Etter du testet positiv, har du nå plager som du ikke hadde før Covid-19? ☐ Nei ☐ Ja

→ Hvis ja, hvilke symptomer (vennligst kryss av):

☐ Feber
☐ Tung pust
☐ Prikking/nummenhet i armer/ben/kropp
☐ Hodepine
☐ Svimmelhet
☐ Hjertebank
☐ Hoste
☐ Redusert lukte/smakssans
☐ Søvnproblemer
☐ Brystsmerter
☐ Muskel eller leddsmerter
☐ Kvalme
☐ Oppkast
☐ Diarre

Andre symptomer: _____

2. Har du blitt covid-smittet på nytt? ☐ Nei ☐ Ja

→ Hvis ja, når: _____

Spørsmålene nedenfor gjelder symptomer nå:

3. Har du problemer med at du føler deg sliten?

☐ Mindre enn vanlig ☐ Ikke mer enn vanlig ☐ Mer enn vanlig
☐ Mye mer enn vanlig

4. Har du vansker med å konsentrere deg?

☐ Mindre enn vanlig ☐ Som vanlig ☐ Mer enn vanlig
☐ Mye mer enn vanlig

5. Hvordan er hukommelsen din?

☐ Bedre enn vanlig ☐ Ikke verre enn vanlig ☐ Verre enn vanlig
☐ Mye verre enn vanlig

6. Hvis du har dårlig hukommelse, konsentrasjonsvansker eller er sliten for tiden, omtrent hvor mye av tiden?

☐ 25 % av tiden ☐ 50 % av tiden ☐ 75 % av tiden
☐ Hele tiden

7. Hvis du for tiden har dårlig hukommelse, konsentrasjonsvansker eller er sliten, omtrent hvor lenge har det vart?

☐ < 1 uke ☐ < 3 måneder ☐ 3-6 måneder

☐ 6 måneder eller mer

8. Har du følt deg nedfor og deprimert?

☐ Mindre enn vanlig ☐ Ikke mer enn vanlig ☐ Mer enn vanlig

☐ Mye mer enn vanlig

9. Er du tungpustet?

☐ Mindre enn vanlig ☐ Ikke mer enn vanlig ☐ Mer enn vanlig

☐ Mye mer enn vanlig

10. Har du vært innlagt sykehus? ☐ Nei ☐ Ja

→ Hva var grunnen?: _____

11. Har du vært i kontakt med fastlege eller legevakt på grunn av covid? ☐ Nei ☐ Ja

→ Hvis ja, hvor mange ganger: _____

12. Var du borte fra jobb på grunn av covid? ☐ Nei ☐ Ja

→ Hvis ja, hvor mange dager:

100% fravær - antall dager _____
75-95% fravær - antall dager _____
50-70% fravær - antall dager _____
30-45% fravær - antall dager _____
20% fravær - antall dager _____

13. Var andre voksne i familien din borte fra jobb? ☐ Nei ☐ Ja

→ Hvis ja, hvor mange dager: _____

EQ-5D-5L validert skjema

Under hver overskrift ber vi deg krysse av den ENE boksen som best beskriver helsen din I DAG.

GANGE

☐ Jeg har ingen problemer med å gå omkring

☐ Jeg har litt problemer med å gå omkring

☐ Jeg har middels store problemer med å gå omkring

☐ Jeg har store problemer med å gå omkring

☐ Jeg er ute av stand til å gå omkring

PERSONLIG STELL

☐ Jeg har ingen problemer med å vaske meg eller kle meg

☐ Jeg har litt problemer med vaske meg eller kle meg

☐ Jeg har middels store problemer med å vaske meg eller kle meg

☐ Jeg har store problemer med å vaske meg eller kle meg

☐ Jeg er ute av stand til å vaske meg eller kle meg

VANLIGE GJØREMÅL *(f. eks. arbeid, studier, husarbeid, familie- eller fritidsaktiviteter)*

☐ Jeg har ingen problemer med å utføre mine vanlige gjøremål

☐ Jeg har litt problemer med å utføre mine vanlige gjøremål

☐ Jeg har middels store problemer med å utføre mine vanlige gjøremål

☐ Jeg har store problemer med å utføre mine vanlige gjøremål

☐ Jeg er ute av stand til å utføre mine vanlige gjøremål

SMERTER/UBEHAG

☐ Jeg har verken smerter eller ubehag

☐ Jeg har litt smerter eller ubehag

☐ Jeg har middels sterke smerter eller ubehag

☐ Jeg har sterke smerter eller ubehag

☐ Jeg har svært sterke smerter eller ubehag

ANGST/DEPRESJON

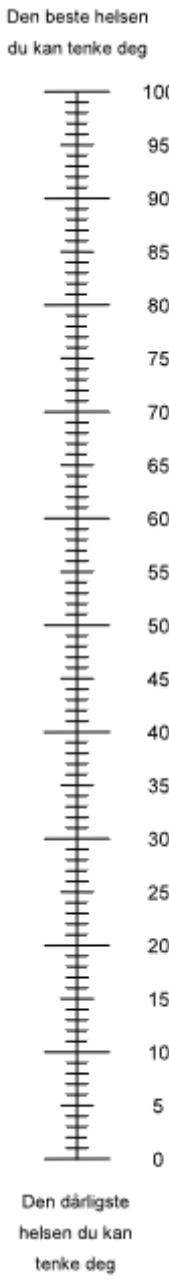
☐ Jeg er verken engstelig eller deprimert

☐ Jeg er litt engstelig eller deprimert

☐ Jeg er middels engstelig eller deprimert

☐ Jeg er svært engstelig eller deprimert

☐ Jeg er ekstremt engstelig eller deprimert



· Vi vil gjerne vite hvor god eller dårlig helsen din er I DAG.

· Denne skalaen er nummerert fra 0 til 100.

· 100 betyr den beste helsen du kan tenke deg. 0 betyr den dårligste helsen du kan tenke deg.

· Sett en X på skalaen for å angi hvordan helsen din er I DAG.

· Skriv deretter tallet du merket av på skalaen
inn i boksen nedenfor.

Helsen din i dag: _____