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Participant Information Sheet/Consent Form – Adult

Title	An International Multi-Centre Randomised Clinical Trial to Assess Clinical, Virological and Immunological Outcomes in Patients Diagnosed with SARS-CoV-2 infection (COVID-19).
Short Title	Australasian COVID-19 Trial (ASCOT)
Protocol Number	ERM62646
Project Sponsor	University of Melbourne
Coordinating Principal Investigators	A/Professor Steven Tong A/Professor Justin Denholm Professor Joshua Davis
Site Principal Investigator	*[Principal Investigator]*
Associate Investigators	*[Associate Investigator(s)]*
Location	*[Location]*

We are inviting you to take part in a research study. Please read this information which will help you decide.

1. Introduction

- You have been diagnosed with Coronavirus Disease 2019 (COVID-19). This is a new type of infection and the best treatments are not yet known.
- This Participant Information Sheet tells you about the research project. It explains the tests and treatments involved. Knowing what is involved will help you decide if you want to take part in the research.
- Participation in this research is voluntary. If you don't wish to take part, you don't have to. You will receive the best possible care whether or not you take part.
- If you decide you want to take part in the research project, you will be asked to sign the consent section. By signing it you are telling us that you:
  - Understand what you have read
  - Consent to take part in the research project
  - Consent to have the tests and treatments that are described
  - Consent to the use of your personal and health information as described.
- You will be posted/emailed a copy of this Participant Information and Consent Form to keep.

2. Why are we doing this study?

- The aim of this study is to try to find the most effective treatments for COVID-19.
- There are two types of treatments (domains) ASCOT is investigating:
  1. Antiviral drugs that aim to stop the virus from replicating;
  2. Convalescent plasma, which is a blood product from donors that have recovered from COVID-19 and that contain antibodies against the COVID-19 virus.

- Your hospital may be participating in investigating one or both types of treatment.
- You may decide to participate in one or both (if available) types of treatment domains.

Antiviral drugs

- In this clinical study, we are trialling 2 antiviral drugs.
- The two drug treatments that will be used in this study have been shown to kill COVID-19 in laboratory tests. The drug names are Lopinavir/ritonavir and hydroxychloroquine.
- You may have seen news reports in June 2020 about hydroxychloroquine, in particular one study published in the Lancet which said that this drug was associated with a higher death rate in COVID-19 patients. This publication was found to be fraudulent and was retracted from publication. The ASCOT investigators, the Melbourne Health Human Research Ethics Committee, and other governing committees unanimously agreed at that time that ASCOT should continue to recruit participants to hydroxychloroquine. Your doctor or treating team would be happy to answer any questions you may have about this.
- In a couple of recent clinical trials, hydroxychloroquine has not been effective against COVID-19 when taken by itself as a single treatment therapy. In this study, hydroxychloroquine will be added to lopinavir/ritonavir.
- Lopinavir/ritonavir is approved in Australia to treat HIV infection. Hydroxychloroquine is approved in Australia to treat inflammatory conditions such as rheumatoid arthritis or Lupus (autoimmune diseases). These 2 drugs are not approved to treat COVID-19. Therefore, both are considered experimental treatments that are being tested to see if they are effective treatments for COVID 19.

Convalescent plasma

- Individuals who recover from COVID-19 develop natural defences to the disease in their blood (called antibodies). Antibodies are found in the part of the blood called plasma. Plasma collected from individuals who have recovered from COVID-19 (called convalescent plasma) will contain antibodies directed against the virus that causes COVID-19. Transfusing convalescent plasma may help patients who are unwell with the SARS-CoV-2 infection. There are trials currently evaluating whether this type of intervention is effective and safe.
- The use of convalescent plasma therapy is considered experimental treatment. This means that it is not an approved treatment for COVID-19 in Australia.

3. What will the study involve?

- You will be told about the study by the Principal Investigator, or a member of the study team, and will have the opportunity to ask any questions.
- The study treatment domains described below are options at this hospital: *[Site to delete which treatment domain they are not participating in.]*
  - Treatment Domain 1 – Antiviral therapy vs standard of care
  - Treatment Domain 2 – Convalescent plasma vs standard of care
- You will have time to decide whether you would like to participate in one or both (if available) of these treatment domains or not.
- You will then be asked to give your verbal consent.

[Delete the next bullet point if study site not participating in research sampling]

- You will also be asked to provide additional verbal consent for the collection of study samples (blood, stool) during the research project.
- We will let your GP know that you have decided to take part in this study.

- All participants will receive standard supportive therapy chosen by their doctor. This includes close monitoring, and treatments such as inhaled oxygen if needed.
- For each treatment domain, you will be randomly allocated by a computer (like drawing straws) to one of the treatment groups below:*[Site to delete which treatment domain they are not participating.]*

Treatment Domain 1: Antivirals

Group 1

Standard supportive therapy.

OR

Group 2

Lopinavir 400mg/ritonavir 100mg, two tablets twice a day for 10 days.

OR

Group 3#

Lopinavir 400mg/ritonavir 100mg, two tablets twice a day for 10 days.

Plus

Hydroxychloroquine (also known as Plaquenil) - four tablets (800mg) two times on day 1, and then two tablets (400mg) twice a day for 6 days.

#If you have kidney disease, your doses of hydroxychloroquine will be lowered to four tablets (800mg) two times on day 1, and then two tablets (400mg) once a day for 6 days.

Treatment Domain 2: Convalescent Plasma

Group 1

Standard supportive therapy.

OR

Group 2

2 units (250 – 310 mL) of blood group compatible convalescent plasma will be given over a 1-2 day period.

- We will collect information recorded as part of your normal care – like your medical history, your temperature and oxygen levels, any chest X-rays and blood tests you may have. Any data recorded from chest imaging will be from tests that have been performed as part of your standard of care, we will not be performing any extra x-rays.
- If you are discharged from hospital, we will contact you by phone or in person, to see how you are going on days 8, 11, 16, 28 and 90 after you enter the study. If we can't reach you, we will call your GP.

[Delete the next 3 bullet points if study site not participating in Treatment Domain 1 Antivirals].

- As well as the standard tests your doctors will do as part of your care, you will have an electrocardiogram (ECG) on days 1, 2 and 4 to monitor your heart rhythms.
- We will measure your blood sugar level on day 2, just before the ECG test. This test is known as a finger prick test and only one drop of blood from your finger is needed.
- When we contact you by telephone, we will check how many tablets of study drug you have left in the bottle. If you are able to, we will also ask you to either email or take a photo of your participant diary and send the images back to the site as a record.

[Delete the next bullet point if study site not participating in Treatment Domain 2 Convalescent Plasma].

- You will need to undergo a blood screen before you receive any convalescent plasma. This is part of normal care and is required to ensure that the plasma is compatible with your blood.
- You will have specific blood tests (to determine the antibody levels) on day 1 before the first transfusion, 24 hours after the second transfusion, and at day 10. If you have been discharged from hospital before day 10, then the study staff will arrange for the day 10 blood test to be collected from you while you recover at home.

[Enhanced and/ Research biological sampling - delete the next 2 bullet points if study site not participating.
- If site is participating in only the PK portion of the study, remove bullet point 1 then remove the wording 7, 15 and 28 while you are in hospital only in bullet point 2;
- sites not involved in PK testing remove day 2 from bullet point 2:]

- We will collect a research specific stool sample on day 1.
- You will have extra blood tests on days 1, 2, 3, 7, 15 and 28 while you are in hospital only. These blood tests are for research purposes only.

4. Do I have to take part in this research project?

- If you do not want to take part in this research, that's OK. Your decision will not affect the quality of care you receive at *[institution]*. If you take part, you are free to withdraw at any time without giving a reason. No further study information will be collected.
- If you decide not to take part, you will receive the usual treatments given to patients with COVID-19 at *[institution]*.

5. What are the benefits of taking part?

- You may or may not benefit from the treatment you receive in this study. A benefit of taking part is that you will receive additional testing and monitoring of your condition which may on its own contribute to an improved health outcome.
- This research will improve our knowledge of how to treat COVID-19 and may improve the care of patients with COVID-19 in Australia, New Zealand and across the world.
- There are no costs involved in taking part in this research, nor will you be paid.

6. What are the possible risks and disadvantages of taking part?

Medical treatments often cause side effects. You may have none, some, or all the effects listed below, and they may be mild, moderate or severe. If you have any of these side effects, and are worried about them, talk with your study doctor. Your study doctor will also be looking out for side effects.

[Delete the next 3 bullet points if study site not participating in Treatment Domain 1 Antivirals].

- For lopinavir/ritonavir, common side effects are diarrhoea, changes in laboratory tests, headache, difficulty in sleeping, lack of strength and energy, nausea, vomiting, abdominal pain, abnormal stools, indigestion, wind, problems with your digestive tract, pain, rash, acne and tingling (prickling or numbness of the skin).

  Uncommon, but more serious side effects are difficulty in breathing, thirst, frequent urination, blurred vision, weight loss, joint stiffness, aches and pains and difficulty in movement, muscle pain, tenderness or weakness.

  The dose of lopinavir/ritonavir you receive will be the standard dose used to treat HIV.

- For hydroxychloroquine, common side effects are nausea, vomiting, diarrhoea, abdominal cramps, loss of appetite, muscle weakness, dizziness, ringing in the ears, headache, nervousness, skin rash, itching and hair loss.

  Other COVID-19 studies have reported that hydroxychloroquine may change the heart's rhythm. In rare cases this may be life threatening but in this study we will closely monitor you for this.

  Uncommon, but more serious side effects are visual disturbances, any hearing loss, suicidal behaviour, frequent fevers, severe chills, sore throat or mouth, severe symptoms of low blood sugar including disorientation, seizures or fits, loss of consciousness.

  As the dose of hydroxychloroquine is higher than the standard dose used to treat malaria, it may cause more side effects. After 1 day, the dose will be dropped.
- Giving both treatments together may cause extra side effects that we do not know about and that may be serious.

[Delete the next 3 bullet points if study site not participating in Treatment Domain 2 Convalescent Plasma].

- For Convalescent Plasma, the table below outlines the common side effects and how likely they are to occur are described in the table below.
- Uncommon = (1-10%) or 1 to 10 people out of every 100 people will report this side effect;
  Rare = (0.1-1%) or 1 in 1,000 to 1 in 100 people will report this side effect;
  Very rare = (<0.1%) or less than 1 in 1,000 people will report this side effect.

Side effect	**How often is it likely to occur**	**Comment**
Rash and itch	Uncommon	Normally self resolves, sometimes antihistamines may be given
Fever	Rare	Normally, self resolves, sometimes antihistamines may be given
Severe allergic reactions	Very rare	Like anaphylaxis and may cause difficulties with breathing and drop in blood pressure
Fluid overload causing difficulty in breathing	Rare	More likely with larger volumes of blood product
Lung injury causing difficulty breathing	Very rare	Risk is reduced by only using plasma from male donors
Infection from the plasma donor	Very rare	All convalescent plasma is stringently screened for infections as per any blood product

- Further details about adverse effects from plasma transfusion can be found at https://transfusion.com.au/adverse_transfusion_reactions/classification_and_incidence.
- If a severe side effect occurs, your doctor may need to stop your treatment. He or she will discuss the best way of managing any side effects with you.
- A possible risk is that using the randomised treatment may require stopping one or more of your usual medications, which may cause unrelated existing conditions to become worse.
- Your doctor will monitor you closely for any changes caused by the treatment you receive.

7. What will happen to the information collected for this study?

- Your information will be kept strictly confidential. Study information will be stored securely, and access will be restricted only to study staff at *[institution]*.

- The only people allowed to look at information that could identify you will be your doctors, study staff, authorised representatives of the Sponsor and regulatory authorities who may want to check that the study is being carried out correctly.
- Information about you may be obtained from your health records held at this and other health services for the purpose of this research.
- Information collected for the study will be stored securely at *[institution]* for 15 years after the study has ended and is the responsibility of the Principal Investigator.
- Information that has had personal identifiers removed (e.g. your name and personal details) will be replaced with a unique study code. This information will be entered by study staff into a database kept at Peter MacCallum Cancer Centre, Melbourne.
- The University of Melbourne (Sponsor) will be responsible for maintaining the confidentiality of the information in the database.

8. What will happen to my research samples?

- The results of routine tests taken as part of your usual care will be available to the study doctors through your hospital medical record.
- With your consent, we would like to store the samples from these routine tests in a central laboratory indefinitely (for example throat/nose swab). This is so they can be used for potential future research about COVID-19 and related conditions.
- You do not need to agree to the storage of your samples in order to take part in this study.
- Your samples and any paperwork with the samples will not be able to identify you. Your personal information will be removed.

[For Victoria, SA and Tas keep the next bullet point. All other states remove]

- Samples will be stored in a central laboratory at the Doherty Institute in Melbourne.

[Victoria, SA and Tas remove next bullet point. All other states complete details]

- Samples will be stored in a central laboratory within *[name facility in state]*. The Doherty Institute in Melbourne will supervise the sample storage.

[Remove the next 7 bullet points if the institution is not involved in optional research parts of the study.]

- With your consent, any extra research samples obtained as part of this study will be stored in the central laboratory indefinitely. This is so they can be used for potential future research about COVID-19 and related conditions.
- It is not possible to predict exactly what specialised laboratory tests will be performed on your samples. Tests will focus mainly on the immune system and responses, as well as studying the virus that caused your COVID-19 illness.
- With your consent, one sample may be used for genetic research that involves ''whole genome* sequencing''. It will look for the areas of your genome that may play a role in the development of COVID-19.

  *The genome is the body's "instruction manual". It contains all the information needed to make you, run you and repair you. You have a copy in nearly every cell in your body. It is made up of a chemical code called DNA, and there are 3 billion letters of code.
- This research is looking at all the letters of this code (whole genome sequencing). The research will look at finding the genetic areas which are susceptible to COVID-19 when compared with healthy people.
- Your sample will be one of many and the genetic research is limited. It will not provide any information about your future health or risk of having children with a genetic disorder, or information that may be relevant to the health of family members who are not part of this study.

- You will not be given the results of your individual research results. This research study is not intended to provide you or your treating doctor with clinical information, or impact on your clinical treatment.

9. Could the research study be stopped unexpectedly?

- This research project may be stopped unexpectedly for a variety of reasons. These may include reasons such as:
  - Unacceptable side effects;
  - The drug(s) and/or convalescent plasma are shown not to be effective;
  - The drug(s) and/or convalescent plasma are shown to work and not need further testing.

10. Can I have other treatments during this research?

- Whilst you are in this research, you may not be able to take some or all of the medications or treatments you have been taking for other reasons.
- It is important to tell your study doctor and the study staff about any treatments or medications you may be taking.
- Your study doctor will consult with your specialist, before explaining which treatments or medications may need to be stopped or changed for the time you are on the study.

11. Who is organising this study?

- The study is being sponsored by the University of Melbourne.
- The study is being coordinated by the Peter Doherty Institute for Infection and Immunity, a joint venture between the University of Melbourne and Royal Melbourne Hospital (Doherty Institute), as well as the Australasian Society for Infectious Diseases Clinical Research Network and will involve about 2000 participants in over 50 hospitals in Australia and New Zealand.
- The study has been funded by a number of organisations including government, charitable donations and through private donations.

12. What happens when the research project ends?

- At the end of the trial, which should be in 2 years, we can send you a summary of the research results on request.

13. Complaints and compensation

- If you suffer any injuries or complications as a result of this research project, you should contact the study team as soon as possible who will help arrange any medical treatment you may need. If you are eligible for Medicare, you can receive any medical treatment required to treat the injuries free of charge, as a public patient in any Australian public hospital.
- In the event of loss or injury, the Sponsor has agreed to pay for hospitalisation and any medication costs.
- You will not be giving up your legal rights by signing this consent form.

14. Who has reviewed the research project?

- The ethical aspects of this research project have been approved by the Human Research Ethics Committee (HREC) of Melbourne Health. This project will be carried out according to the

National Statement on Ethical Conduct in Human Research (2018). This statement has been developed to protect the interests of people who take part in research studies.

15. Further information and who to contact

- The person you may need to contact will depend on your query. If you want more information about this project, you can contact the lead study doctors: Associate Professor Steven Tong on (03) 9342 9406, Associate Professor Justin Denholm on justin.denholm@mh.org.au or Professor Joshua Davis on joshua.davis@menzies.edu.au.

For questions about your medical care or about taking part in the trial at this hospital:

Clinical contact person

Name	*[Name]*
Position	*[Position]*
Telephone	*[Phone number]*
Email	*[Email address]*

The HREC that has approved this research and HREC Executive Officer details

Reviewing HREC name	Melbourne Health HREC
HREC Executive Officer	Complaints Manager
Telephone	(03) 9342 8530
Email	research@mh.org.au

Site - Research Governance Officer

Name	*[Name]*
Position	*[Position]*
Telephone	*[Phone number]*
Email	*[Email address]*

Consent Form - Adult providing own consent

Title	An International Multi-Centre Randomised Clinical Trial to Assess Clinical, Virological and Immunological Outcomes in Patients Diagnosed with SARS-CoV-2 infection (COVID-19).
Short Title	Australasian COVID-19 Trial (ASCOT)
Protocol Number	ERM62646
Project Sponsor	University of Melbourne
Coordinating Principal Investigators	A/Professor Steven Tong A/Professor Justin Denholm Professor Joshua Davis
Site Principal Investigator	*[Principal Investigator]*
Associate Investigator(s)	*[Associate Investigator(s)]*
Location	*[Location]*

Verbal Declaration by Participant

- I have read the Participant Information Sheet, or someone has read it to me in a language that I understand.
- I understand the purposes, procedures and risks of the research described in the project.
- I have had an opportunity to ask questions and I am satisfied with the answers I have received.
- I freely agree to participate in this research project as described and understand that I am free to withdraw at any time during the project without affecting my future health care.
- I give permission for my doctors, other health professionals, hospitals or laboratories outside this hospital to release information to *[institution]* concerning my condition and treatment for the purposes of this project. I understand that such information will remain confidential.
- I consent to participating in Treatment Domain 1 Antivirals ☐ Yes ☐ No
  [delete if hospital site not participating in Treatment Domain 1]
- I consent to participating in Treatment Domain 2 Convalescent plasma ☐ Yes ☐ No
  [delete if hospital site not participating in Treatment Domain 2]
- I consent for the use of my collected information in future research. ☐ Yes ☐ No
- I understand that I can withdraw my consent to participate in the research project by filling in a "Withdrawal of Consent" form, or by telling a study team member.
- I would like a copy of the study results when they become available. ☐ Yes ☐ No

Name of Participant (please print) _____

Email address *(if participant would like results emailed):* _____

Name of Interpreter if used _____

Signature _____ Date _____

☐ Consent was obtained using interpretation via telephone and whose photographic identification was sighted by the Investigator.

Declaration by Study Doctor/Senior Researcher†

I have given a verbal explanation of the research project, its procedures and risks and I believe that the participant has understood that explanation.

Name of Study Doctor/
Senior Researcher† (please print) _____

Signature _____ Date _____

† A senior member of the research team must provide the explanation of, and information concerning, the research project.

[Remove the next 2 bullet points, and extra declarations if the institution is not involved in research testing parts of the study.]

- I consent to the storage and use of blood and tissue samples taken from me for use, as described in the related section of the Participant Information Sheet, for
  - This specific research study ☐ Yes ☐ No
  - Other research study that is closely related to this research project ☐ Yes ☐ No
  - Any future research ☐ Yes ☐ No
- In respect to the storage and use of my DNA samples, I give permission for the use of my DNA samples for the purpose of
  - This specific research study ☐ Yes ☐ No
  - Other research study that is closely related to this research project ☐ Yes ☐ No
  - Any future research ☐ Yes ☐ No

Name of Interpreter if used _____

Signature _____ Date _____

☐ Consent was obtained using interpretation via telephone whose photographic identification was sighted by the Investigator.

Declaration by Study Doctor/Senior Researcher†

I have given a verbal explanation of the research project, its procedures and risks and I believe that the participant has understood that explanation.

Name of Study Doctor/
Senior Researcher† (please print) _____

Signature _____ Date _____

† A senior member of the research team must provide the explanation of, and information concerning, the research project.

A copy of this consent will be sent/emailed to the participant