CONTROL COVID

CONTROL OF COVID-19 OUTBREAKS IN LONG TERM CARE

CONSENT TO PARTICIPATE IN A RESEARCH STUDY

Title	Control of COVID-19 outbreaks in long term care (Control-COVID)
Protocol No:	CONTROL-COVID-Favipiravir-1
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Sponsor	Appili Therapeutics

Introduction

This consent form is intended for the resident who is eligible to take part in the study. Please note the use of the term 'you' in this form refers to the eligible resident. However if the resident, is incapable of providing consent due to severity of illness, the consent of a substitute Decision Maker (SDM) will be sought.

You are being asked to take part in a research study. Please read this explanation about the study and its risks and benefits before you decide if you would like to take part. You should take as much time as you need to make your decision. However, if you are making a decision after an outbreak has started, you will need to make a decision about whether you agree to take the study drug or not within 24 hours of our contacting you in order to prescribe study drug as soon as possible. You should ask the study doctor or study staff to explain anything that you do not understand and make sure that all of your questions have been answered before signing this consent form. Before you make your decision, feel free to talk about this study with anyone you wish. Participation in this study is voluntary.

Background

- You have been asked to take part in this research study because someone on a unit in the long term care facility in which you reside has become ill with the novel coronavirus (COVID-19) and it is possible that you have been exposed to the virus.
- COVID-19 is a new infection caused by a virus. You can get COVID-19 through contact with another person who has the virus.
- COVID-19 is spreading throughout Canada, including in long term care homes.

- COVID-19 causes illness that ranges from mild (an upper respiratory tract illness with runny nose, aching and/or cough) to an illness with fever and cough that can last for 2-3 weeks, to severe pneumonia, which can result in death. In young, healthy people, severe disease requiring hospital admission is uncommon (less than 1 in 50), but does occur.
- COVID-19 is much more severe in the elderly, with significantly higher rates of complications and death. It is particularly severe in residents of long term care; as many as 3 in 10 residents may die of the infection.
- There is no specific medication proven to prevent or treat COVID-19.
- The usual standard of care for COVID-19 outbreaks in long term care homes is to test all residents and health care providers on the affected unit to see if they have been infected with the virus, to limit visitors and limit movement of residents and staff in the home, to increase cleaning, and to use additional precautions such as masks and gloves. The decisions about what control measures will be taken during this outbreak will be made by the administration of the home and your local public health unit. They will not be changed in any way because of this study.
- Unfortunately, these measures may not be enough to control outbreaks of COVID-19 or prevent disease in people who are already exposed to the virus. Outbreaks of COVID-19 are occurring in long term care homes across the country, resulting in severe outcomes. Identifying additional options to control outbreaks of COVID-19 in long term care is very important.

Purpose

- This study will assess whether giving a drug called favipiravir to residents and staff can be used to help control outbreaks of COVID-19 infection in long term care homes.
- Favipiravir is a drug which is approved in Japan and China for the treatment of influenza, and has been tested in studies against other viral illnesses.
- Favipiravir is not approved for routine use in Canada, but has been approved for research use in this study.
- Approximately 400 residents from 16 long term care homes, and the staff who take care of them will be included in the study.
- We hope to improve the control of current and future COVID-19 outbreaks in long term care homes.

Study Design

- For residents, this study compares the effects of favipiravir to a placebo. A placebo looks like the study drug but contains no active medication.
    - If you have tested positive for COVID-19 or test positive on day 0, you will receive either favipiravir or placebo: 10 tablets twice a day on day 1, then 5 tablets twice daily for 14 days.
    - If you test negative for COVID-19, you will receive either favipiravir or placebo 8 tablets twice daily on day 1 then 4 tablets twice daily until day 25.
- This is a cluster-randomized, multi-centre, blinded clinical trial.
- Definitions:
    - Randomized: Whether you get the study drug or the placebo will be decided randomly (by chance) like rolling a dice. There is a 1 in 2 chance of receiving favipiravir.
    - Cluster: All residents of the long term care home unit will receive the same medication.
    - Multi-centre: Multiple long term care homes will be involved in the study.

- Blinded: This means that you will not be told whether you are receiving favipriavir or placebo until the study is finished. No one except the person doing the randomization will know which one you received. This information can be revealed in case of an emergency.
- You will be in the study for a total of 60 days.

Study Contacts and Procedures

Initial contact: You will be contacted by telephone to determine if you are eligible to participate in the study: The following will occur at this time:

- You will be asked some questions about your current medications and health history to determine whether you can safely take the study drug.
- The study staff will also go through this informed consent form with you by telephone
- Study staff will then review your health history and medications with long term care home staff to confirm that you are eligible to take study medication
- If you are not eligible to take the study medication, or choose not to, we will still ask that consider being a part of the study so that we can follow you to find out if you have COVID-19 as part of this outbreak.
- If you consent to participate in the study, your contact information will be obtained.
- If you have not already been required to submit a nasal swab for testing as part of standard outbreak control measures, staff at the long term care home or study staff will obtain a nasal swab which will be tested for COVID-19. You will be informed of the result.

Randomization: The randomization procedure will occur electronically. If you consent to participate in this research study, you will be assigned to either take favipiravir or placebo for the duration of 25 days.

Start of prophylaxis (day 1):

- If you are eligible and choose to take study drug, you will start taking it twice daily. Your study drug will be administered by staff of the long term care home just as your regular medications are.
- Staff of the long term care home will check on you as usual. If you have any symptoms of COVID-19, they will send a nasal swab for testing.

Daily follow up assessment day 2-40:

- During study days 2 to 40, the staff at your long term care home will check on you regularly as they usually do.
- If you have symptoms of COVID-19, they will send a swab for testing.
- If you have other symptoms, the home staff will call the study. They will also call your doctor as usual if they need to. If your doctor or the study staff believe that your study medication needs to be discontinued, your doctor and a study doctor will discuss this. If, after the discussion, either the study doctor or your doctor believe that the medication should be discontinued, it will be. You will be notified if this happens.
- If you develop illness severe enough to require hospitalization, you will be cared for as usual by doctors and nurses in the hospital. They will make the decision with you about whether or not the study medication is continued.

Follow up assessment #1 (day 14):

- Study staff will review your status and symptoms with you and with staff of the long term care home and will review your nursing notes to assess whether you have had any symptoms, or been tested for COVID-19, and – if you are taking study medication - about whether you have had any symptoms that might be due to the study medication.
- A member of the study staff will ask you if they can take a nasal swab.

Follow up assessment #2 (day 40)

- Study staff will review your status with you and with staff of the long term care home and will review your nursing notes to assess whether you have had any symptoms, or been tested for COVID-19, and – if you are taking study medication - about whether you have had any symptoms that might be due to the study medication.
- A member of the study staff will ask you if they can take a nasal swab.

Follow-up assessment #3 (day 60)

- Study staff will review with you and with staff of the long term care home and will review your nursing notes to assess if you have experienced any adverse events, hospitalizations or have died during the study period

Calendar of Participant Contacts

Boxes marked with an X show what will happen at each time during the study:

Visit	**Screening (Day 0)**	**Baseline (Day 1)**	**Day 14± 2d**	**Day 40± 4d**	**Day 60± 7d**
Visit format	**Remote (ex. NP)**	**Remote**	**In person**	**In person**	**Remote or in person**
Eligibility assessment	**X**				
Informed consent	**X**				
Cluster randomization		**X**			
Dispensing study drugs		**X**			
Assessment for COVID-19		**Daily, by LTC staff (fax to study) Chart review by study staff, day 14 &40**			
Concomitant medication assessment	**X**		**X**	**X**	
Adverse event assessment		**Daily by LTC staff (fax to study) Chart review by study staff, day 14 & 40**			**SAE only**
Death/hospital transfer documentation		**Daily by LTC staff (fax to study) Chart review by study staff, day**			**X**

		14 & 40			
Nasopharyngeal/nasal swab	**X**		**X**	**X**	
Medication adherence			**X**	**X**	
Time	**30-40 minutes**	**5 minutes**	**15-20 minutes**	**15-20 minutes**	**10-15 minutes**

Reminders
It is important to remember the following things during this study:

- Ask your study team about anything that worries you.
- Tell study staff anything about your health that has changed.
- Tell your study team if you change your mind about being in this study.

Risks Related to Being in the Study

This study has risks. Some of these risks we know about. There is also a possibility of risks that we do not know about and have not been seen in study subjects to date. Some can be managed. Please call the study doctor or inform your care provider if you have any side effects even if you do not think it has anything to do with this study.

The risks related to taking favipiravir that we know of are (the numbers in brackets show how often the side-effects happened):
Serious: No serious side-effects related to taking favipiravir have been noted in licensure studies in Japan or the United States.
Very Common: (≥ 10%) There are no very common side effects.
Common: (≥1% but <10%) Diarrhea, nausea, vomiting, elevated triglyceride levels in blood, elevated liver enzymes, headache.
Very Rare: Mild to moderate changes to uric acid and aminotransferase have been observed. These changes have reversed when favipiravir is discontinued.

Risks Related to Pregnancy and breastfeeding
Favipiravir may cause birth defects in unborn babies. If you are a woman of childbearing years, you should not take favipiravir.

Benefits to Being in the Study

You may or may not receive direct benefit from being in this study. Information learned from this study may help other long term care homes with COVID19 outbreaks in the future.

Voluntary Participation

Your participation in this study is voluntary. You may decide not to be in this study, or to be in the study now and then change your mind later. You may leave the study at any time without affecting your care in any way. You may refuse to answer any question you do not want to answer, or not answer an interview question by saying "pass".

We will give you new information that is learned during the study that might affect your decision to stay in the study.

Confidentiality

Personal Health Information

If you agree to join this study, the study doctor and his/her study team will ask about your personal health information and collect only the information they need for the study. Personal health information is any information that could be used to identify you and includes your:

- name,
- address,
- date of birth,
- new or existing medical records, that includes types, dates and results of medical tests or procedures.

The information that is collected for the study will be kept in a locked and secure area by the study doctor for 25 years. Only the study team or the people or groups listed below will be allowed to look at your records. Your participation in this study also may be recorded in your medical record at the nursing home.

The following people may review the study records and your personal health information to check that the information collected for the study is correct and to make sure the study followed proper laws and guidelines. They are:

- The study sponsors or its representatives/partner companies.
- Representatives of the Mount Sinai Hospital Research Ethics Board.
- Representatives of Health Canada, or other regulatory bodies (groups of people who oversee research studies) outside of Canada, such as the United States Food and Drug Administration.

Study Information that Does Not Identify You

Some study information will be sent outside of the study to the Sponsors. Any information about you that is sent out will have a unique study code and will not show your name or address, or any information that directly identifies you.

The Sponsors may use the study information and share it with its partner companies or with national and international regulatory agencies to help answer the study question, to get approval to sell favipiravir, to develop future studies on this product or for research related to this study.

All information collected during this study, including your personal health information, will be kept confidential and will not be shared with anyone outside the study unless required by law.

You will not be named in any reports, publications, or presentations that may come from this study.

If you decide to leave the study, the information about you that was collected before you left the study will still be used. No new information will be collected without your permission.

Clinical Trial Registration

A description of this clinical trial will be available on http://www.ClinicalTrials.gov. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

In Case You Are Harmed in the Study
If you become ill, injured or harmed as a result of taking part in this study, you will receive care. The reasonable costs of such care will be covered for any injury, illness or harm that is directly a result of being in this study. In no way does signing this consent form waive your legal rights nor does it relieve the investigators, sponsors or involved institutions from their legal and professional responsibilities. You do not give up any of your legal rights by signing this consent form.

Expenses Associated with Participating in the Study You will not have to pay for any of the study drug involved with this study. You will not receive any remuneration for study participation.

Conflict of Interest
Appili Therapeutics will provide favipiravir and matching placebo for residents and staff in this study without cost. All of these people have an interest in completing this study. Their interests should not influence your decision to participate and you should not feel pressured to join this study.

Questions About the Study
If you have any questions, concerns or would like to speak to the study team for any reason, please call; Dr. Allison McGeer at 416-586-3123 or the study coordinator at 416-586-4800 ext. 2676. You can leave a message at either of these numbers and someone will get back to you as soon as possible. If the situation is urgent, the study can also be reached at any time by calling locating at Mount Sinai Hospital (416-586-5133) and they will connect you with the investigator on call.

If you have any questions about your rights as a research participant or have concerns about this study, call Ronald Heslegrave, Ph.D., Chair of the Mount Sinai Hospital Research Ethics Board (REB) or the Research Ethics office number at 416-586-4875. The REB is a group of people who oversee the ethical conduct of research studies. These people are not part of the study team. Everything that you discuss will be kept confidential.

Statement of Consent for Participant

Study Title: Control of COVID-19 outbreaks in long term care (Control-COVID)

I acknowledge that the research study described above has been explained to me and that any questions that I have asked have been answered to my satisfaction. I have been informed of the alternatives to participation in this study, including the right not to participate and the right to withdraw without compromising the quality of my care at my long term care home. As well, the potential risks, harms and discomforts have been explained to me and I also understand the benefits (if any) of participating in the research study.

I understand that I have not waived my legal rights or released the study doctors, sponsor, or involved institutions from their legal and professional duties. I know that I may ask now, or in the future, any questions I have about the study or the research procedures. I have been assured that records relating to me and my care will be kept confidential and that no information will be released or printed that would disclose my personal identity without my permission unless required by law. I have been given sufficient time to read and understand the above information.

☐ I consent to participate in this study and the use of my personal health information as described above.

☐ I DO NOT consent to take study drug, but I agree to the collection of minimal observational data from my medical chart, and to having study swabs on day 0, day 14 and day 40

I **will** be given a copy of the signed and dated consent form.

Print Study Participant's Name	Signature of Participant	Date

I have explained to the above-named participant the nature and purpose, the potential benefits, and possible risks associated with participation in this research study. I have answered all questions that have been raised about the study.

Print Name of Person Obtaining Consent	Signature	Date

Was the participant assisted during the consent process? ☐**YES** ☐**NO**

If **YES**, please check the relevant box and complete the signature space below:

☐The person signing below acted as a translator for the participant during the consent process and attests that the study as set out in this form was accurately translated and has had any questions answered.

Print Name of Translator	Signature	Date

Relationship to Participant	Language

☐ The consent form was read to the participant. The person signing below attests that the study as set out in this form was accurately explained to, and has had any questions answered.

Print Name of Witness	Signature	Date

Relationship to Participant

STATEMENT OF CONSENT

FOR SUBSTITUTE DECISION MAKER

Study Title: Control of COVID-19 outbreaks in long term care (Control-COVID)

I acknowledge that the research study described above has been explained to me and that any questions that I have asked have been answered to my satisfaction. I have been informed of the alternatives to the below-named participant's participation in this study, including the right not to consent to participation and the right to withdraw him/her without compromising the quality of care for him/her at the long term care home. As well, the potential risks, harms and discomforts have been explained to me and I also understand the benefits (if any) of his/her participating in the research study.

I understand that I have not waived his/her legal rights nor released the study doctors, sponsor, or involved institutions from their legal and professional duties. I know that he/she and I may ask now, or in the future, any questions we have about the study or the research procedures. I have been assured that records relating to him/her and his/her care will be kept confidential and that no information will be released or printed that would disclose personal identity without permission unless required by law. I have been given sufficient time to read and understand the above information.

☐ I hereby consent to his/her participation in this study.

☐ I DO NOT consent to his/her participation in this study but agree to the collection of minimal observational data from his/her medical chart.

I **will** be given a copy of the signed and dated consent form.

Print Name of Study Participant	Print Name of Substitute Decision Maker	

Signature of Substitute Decision Maker	Relationship to Participant	Date

I have explained to the substitute decision maker of the above-named participant the nature and purpose, the potential benefits, and possible risks associated with participation in this research study. I have answered all questions that have been raised about the study.

Print Name of Person Obtaining Consent	Signature	Date

Was the substitute decision maker assisted during the consent process? ☐**YES** ☐**NO**

If **YES**, please check the relevant box and complete the signature space below:

☐The person signing below acted as a translator for the substitute decision maker during the consent process and attests that the study as set out in this form was accurately translated and has had any questions answered.

Print Name of Translator	Signature	Date

Relationship to Participant	Language

☐The consent form was read to the substitute maker. The person signing below attests that the study as set out in this form was accurately explained to, and has had any questions answered.

Print Name of Witness	Signature	Date

Relationship to Participant