UNIVERSITY OF SASKATCHEWAN

ANIMAL OWNER INFORMATION AND CONSENT FORM

STUDY TITLE: Coagulation testing in cats with Feline Infectious Peritonitis before and after treatment with the antiviral GS441524 with the aim to characterize features of a Feline Infectious Peritonitis Associated Coagulopathy and to see if it shares features in common with the coagulopathy seen with Covid-19 pneumonia in people.

PRINCIPAL INVESTIGATOR:
Dr. Elisabeth Snead
BSc, DVM, MSc, Diplomate ACVIM
Small Animal Internal Medicine Specialist
Professor, Department Small Animal Clinical Sciences
Western College of Veterinary Medicine
Director Feline Radioactive Iodine Program
University of Saskatchewan
Phone: 306-966-2700

SUB-INVESTIGATORS:
Jessica Pui Man Lam, Small Animal Internal Medicine Resident, Department Small Animal Clinical Sciences
Mafer Morales Uribe, Small Animal Internal Medicine Resident, Department Small Animal Clinical Sciences

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INTRODUCTION

You are invited to enter *(name of your cat)* _____ in this research study.

Your animal's participation is voluntary; you decide if you want them to take part. If you decide for them to participate in this study, you will be asked to sign this form and you are able to withdraw them at any time without giving any reasons for your decision. If you do not wish your animal to participate, you will not lose the benefit of any veterinary care your animal is receiving.

Please read the following information carefully. We are happy to answer any questions and/or to explain any terms or information that you would like clarification on.

WHO IS CONDUCTING THIS STUDY?

This study is being undertaken by Dr. Snead, Dr. Carr Dr. Lam and Dr. Uribe at the Western College of Veterinary Medicine at the University of Saskatchewan.

WHY IS THIS STUDY BEING DONE?

Feline Infectious Peritonitis (FIP) is a deadly viral disease that affects cats, caused by a type of coronavirus that can lead to serious and often fatal complications until the recent discovery of an antiviral medication. This viral disease typically presents in either a wet or dry form - the wet form involves the accumulation of fluid in body cavities, while the dry form is characterized by the development of mass like lesions in various organs.

Humans with severe Covid 19 pneumonia, also caused by a coronavirus, often develop a coagulopathy referred to as Covid-19 Associated Coagulopathy (CAC) which leads to significant risk of thromboembolic

complications which often involve the lungs and may lead to life-threatening respiratory distress or failure. Very little is known about coagulation abnormalities with cats with spontaneous FIP, but recently abnormal blood clotting has also been noted in a subset of affected cats prior to treatment that were very similar to what is seen in humans with CAC.
The aim of this study is to investigate the mechanisms behind the coagulation problems seen in cats with FIP and determine if there are similarities to the coagulation issues observed in people with severe COVID-19 infections. To accomplish this, select coagulation tests will be performed in 16 cats diagnosed with the wet (8 cats) and dry (8 cats) forms of FIP with the results compared to findings in a group of age and sex matched healthy control cats.

Additionally, the study will assess whether any coagulation problems with FIP are linked to the severity of the cat's illness, respiratory involvement, or chances of survival. The findings will be compared to the coagulation disorder seen in some COVID-19 patients.

By understanding the similarities and differences in the coagulation problems between FIP in cats and COVID-19 in people, this research has the potential to improve the diagnosis and management of these critical blood clotting disorders in both veterinary and human medicine. The findings could lead to better treatments and outcomes for affected patients.

Currently there is only one commercially available antiviral (GS441524) for the treatment cats with FIP This antiviral is efficacious in 80-85% of cases. This antiviral is known to be very safe but rare side effects can occur with any medication. The only known reported side-effects with this antiviral to date include rare liver or kidney issues that resolve once the drug is stopped and very rare bladder stone formation associated with excretion of drug breakdown products in the urine. This study also seeks to measure coagulation parameters before and after therapy with the antiviral GS 441524 in cats with FIP to learn if a 6-week course of therapy resolves any abnormalities detected.

WHICH ANIMALS CAN PARTICIPATE IN THIS STUDY?

Your animal is eligible to participate in this study if he/she has been diagnosed presumptively through their family veterinarian or our small animal internal medicine service with Feline infectious peritonitis (FIP) based on a preponderance of evidence from a standard diagnostic work up (see below for details) and provided your cat has no other exclusion criteria that would interfere with the results of the study.

The work up to establish a diagnosis of FIP will involve basic blood work, retroviral testing, medical imaging (chest radiographs and an abdominal ultrasound) support from molecular test to detect the virus or a high antibody titre to the virus. The costs of these tests unfortunately cannot be covered by the study and must be covered by the owner. The cost of monitoring certain blood work abnormalities on a serum biochemistry panel during treatment also needs to be paid for by the owner along with any complications that may arise from their FIP.

Criteria that would lead to excluding a cat from our study include any of the following: pre-existing inherited coagulopathy; prior diagnosis of cancer; administration of a medication known to directly affect coagulation (including any prior anticoagulant therapy/ or oral / ocular steroids in the last 7 days), physical examination or medical imaging finding that are supportive of underlying primary cardiac disease (Grade III-VI heart murmur, a gallop rhythm or unexplained acquired or congenital heart disease). An echocardiogram may be required to determine if there is pre-existing heart disease and if that is necessary the cost of that would be the responsibility of the owner as part of the diagnostic work up.

We will only be enrolling 16 cats with FIP into this study total (eight with wet FIP and eight with dry FIP) along with 16 healthy age and sex matched control cats. Pets and their owners must be willing to travel to the WCVM at a minimum twice during the study period. Before we can enroll your cat, we will also require a full set of veterinary records to be sent to our office by your family veterinarian.

WHAT DOES THIS STUDY INVOLVE?

For cats with FIP if your pet is eligible to take part in the study, and you choose to enroll them, then the following will happen as part of the study:

1. Blood will be taken after a brief fast before and after 6 weeks of antiviral therapy. Ideally at the midpoint of the treatment period, we would also examine your cat. The follow up visits will allow us to evaluate for important indicators of remission or progression of the disease and to check clotting times after your cat completes a 6-week course of antiviral therapy. The 3 week follow up visit would ideally be done at the VMC but if needed can be done through your family veterinarian, however, the initial and final visit at 6 weeks must be done at the VMC at the WCVM. At the initial and 6 week follow up visit we will take a blood sample to allow for select coagulation tests to be run after injecting a very small volume of a local anesthetic over the site of collection. Whenever possible this may happen at the same time as collection of other blood required to monitor your cat's response to therapy.
2. Weekly assessment of quality of life and measurement of your cat's body weight will be required to be completed at home in order to monitor your cat's response to treatment.

Some cats will only partially respond at the initial antiviral dos. This is often due to the severity of their disease, and this may require a dose increase or in some cases a longer course of therapy. In cats with severe disease at the time of initial diagnosis, they may even fail to respond at all and or sadly die or require humane euthanasia due to quality-of-life issues before treatment can be effective or initiated. There are also cases that relapse after initially responding and that require longer term therapy. If your cat requires more than 6 weeks of this therapy, Dr. Snead will be able to prescribe this but unfortunately the study can only cover a 6-week course of therapy.

You will receive discharge notes that provide details of all our findings and the care we provided along with instructions regarding administration of the antiviral therapy, what to watch for in terms of side-effects and what can be expected with a positive response to therapy. Early signs of remission in response to therapy include rapid resolution of fever, lethargy and an increased appetite. These are all expected within a few days of initiating therapy. Weight gain and resolution of clinical abnormalities (body cavity effusions) will take a few weeks and finally complete resolution of some of the blood work abnormalities (anemia, low lymphocyte count) and lesions in organs seen with imaging are expected to take weeks to months to resolve.

For the healthy age and sex matched cats, the study will fund a full physical examination and an abbreviated CBC and full serum biochemistry panel. You cat will only need to be seen once and at that visit a blood sample will be taken to measure coagulation parameters.

WHAT ARE THE BENEFITS OF PARTICIPATING IN THIS STUDY?

This study will cover the cost of the antiviral therapy, the cost of the coagulation tests, and pay for two follow up CBC in the cats with FIP. Our expertise gained by treating other cats with FIP will also be available throughout the study and afterwards. For the healthy controls the study will pay for a full physical examination and some basic blood work.

It is hoped the information gained from this study can be used in the future to benefit other cats that develop a coagulopathy related to FIP.

WHAT ARE POSSIBLE RISKS AND DISCOMFORTS?

Taking blood does cause a slight pinch or mild pain when the needle is inserted, similarly to when blood is drawn in humans. Most cats, like people, tolerate this without any obvious distress. Use of a small dose of a local anesthetic called bupivacaine administered just under the skin over the vein will be used when collecting the blood sample to help reduce any discomfort.

All drugs have side-effects and it is possible your cat could develop an adverse reaction to the prescribed antiviral GS 441524 but luckily based on lots of published data the drug is very safe and side-effects are rarely reported.

WHAT IF NEW INFORMATION BECOMES AVAILABLE? If during this study, new information that may affect your willingness to continue to let your pet (cat or dog) participate will be provided to you and you will be able to make an informed decision on whether you would like to continue or not to have your pet enrolled in the study.

WHAT HAPPENS IF I DECIDE TO WITHDRAW?
Your animal's participation in this research is voluntary. You may withdraw your animal from this study at any time. You do not have to provide a reason and there will be no penalty of any sort.

If you choose to let your animal enter the study and then decide to withdraw later, all data collected during the time in the study will be retained for analysis.

We do ask that if you do not pursue any form of treatment or if your cat dies from FIP during treatment or fails to respond or that if at any time in the next year you have to make the difficult decision to euthanize your cat regardless of the cause, that you please consider allowing us to conduct a postmortem. This allows us to more thoroughly evaluate the efficacy of the therapy and to correlate any imaging findings with lesions seen in tissues. In some cases, it may also help us establish a definitive diagnosis of FIP if this has not been possible when your cat was living. The cost of this postmortem will be covered by the study.

WHAT WILL THE STUDY COST ME?

You will be responsible for the initial diagnostics, hospitalization and all that is needed to stabilize your pet confirm your cat has FIP and has no concurrent disorders that would exclude their participation.

We will cover the cost of 6 weeks of the antiviral GS 441524 and cover the cost of all the coagulation testing and two complete blood counts done at the 3- and 6-week time points.

Our study will also pay for three vet visits associated with the study if the mid-treatment visit occurs at the VMC.

If your cat is one of the healthy age and sex matched control cats there are no costs other than your time for participating in the study.

You will not be paid for allowing your animal to participate in this study and will be responsible for the cost of any other therapy for dealing with complications of FIP required (e.g. ocular medications, anti-

vomiting medications, appetite stimulant, etc.). All costs for diagnosis, management, and treatment of your animal prior to enrollment and during the study if your cat is seen for any urgent care issue due to their FIP diagnosis or from an unrelated condition will remain your responsibility.

HOW WILL STUDY INFORMATION BE KEPT CONFIDENTIAL?

While absolute confidentiality cannot be guaranteed, every effort will be made to ensure that the information collected for this study is kept confidential. No information that discloses your name or that of your animal will be released or published without your specific consent to the disclosure. Study records will use a numeric code instead of names. Research records identifying you may be inspected in the office and presence of the Principal Investigator by representatives of the funding agency and/or the University of Saskatchewan Animal Research Ethics Board for the purpose of monitoring the research.

All study information will be securely stored in *{name specific physical location}* for a period– 5-years post-publication minimum as per the USask Responsible Conduct of Research Policy, see: https://policies.usask.ca/documents/Responsible_Conduct_Research_Policy__Procedures.pdf.

The results of this study may be presented in a scientific meeting or published in scientific journals, but your identity and that of your animal will not be revealed.

WHO DO I CONTACT IF I HAVE QUESTIONS ABOUT THE STUDY?

If you have any questions or desire further information about this study before or during participation, you can contact
Elisabeth Snead: liz.snead@usask.ca 306-222 -7755

This study has been reviewed and approved on ethical grounds by the University of Saskatchewan Animal Research Ethics Board (AREB). If you have any concerns about the ethical conduct of this study, please contact the AREB at 306-966-7928 or toll-free from outside Saskatoon, 1-888-966-2975.

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CONSENT TO PARTICIPATE

Study Title: Coagulation testing in cats with Feline Infectious Peritonitis before and after treatment with the antiviral GS441524 with the aim to characterize features of a Feline Infectious Peritonitis Associated Coagulopathy and to see if it shares features in common with the coagulopathy seen with Covid-19 pneumonia in people.

- I have read (or someone has read to me) the information in this consent form.
- I understand the purpose and procedures and the possible risks and benefits of the study.
- I was given sufficient time to think about it.
- I had the opportunity to ask questions and have received satisfactory answers.
- I understand that I am free to withdraw my animal from this study at any time for any reason without penalty.
- I give permission to the use and disclosure of de-identified information collected for the research purposes described in this form.
- I understand that by signing this document I do not waive any of my legal rights.
- I have been told I will be given a signed and dated copy of this consent form.
- I am at least 18 years of age and am the legal owner of the animal(s) or authorized to make decisions regarding *{this or these}* animal(s) on behalf of the owner.

I agree to let my animal(s) participate in this study:

Printed name of owner: Signature Date

Printed name of person obtaining consent: Signature Date