Disclaimer: this article is for veterinarians and veterinary students only and for information purposes only. It should NOT be used by non-veterinarians to attempt to treat their own pets. I accept no responsibility whatsover for how you use this information.

10 rules for preventing FIP treatment relapses

- 1. Make sure the FIP diagnosis is correct
- 2. Do <u>NOT</u> use corticosteroids
- 3. Use an oral form of GS-441524, <u>NOT</u> an injectable form and not remdesivir, if possible
- 4. Test faeces for FCoV RNA before starting treatment and one week into treatment to confirm that the antiviral drug works
- 5. Give a 10 day course of double dose of antiviral to clear the brain of virus (longer if the cat is showing neurological signs)
- 6. Remember to increase the antiviral dose as the cat gains weight
- 7. Don't mistake a concurrent disease for treatment failure
- 8. Treat with antiviral drug until two consecutive normal AGP (alpha-1 acid glycoprotein) tests (two normal serum amyloid A tests may also work)
- 9. Eliminate FCoV from in contact cats to prevent re-infection of the patient
- 10. Follow up the anti-viral treatment with 100,000 units of Virbagen Omega by mouth per cat q24h (or 10mg/kg mefloquine 2 or 3 times per week plus zinc picolinate if IFN omega not available)

The precise amongst you will immediately realise that some of the rules (items 1, 7 and 9) are not strictly about preventing relapses, but are about preventing the appearance of a relapse.

INTRODUCTION

There are three possible outcomes when cats are treated for FCoV: complete cure, death or a relapse. Relapse may lead to either cure/remission or death. Many people treating their cats for FIP fear a relapse. It appears to me that as treatment protocols are being refined through the collective experience being shared online, that the frequency of relapses is reducing.

Feline coronavirus (FCoV) specific antivirals fall into two main classes: nucleoside analogues, which interrupt the process of viral RNA being replicated, and 3C-like protease inhibitors, which halt viral replication by inhibiting a major enzyme essential for replication. Examples of the former are GS-441524 (e.g. Mutian, Remdesivir, which is the precursor of GS-442524) and EIDD; and an example of a protease inhibitor is GC376. There are other general antivirals such as interferon, zinc picolinate, mefloquine and ivermectin.

This article will be updated when more information becomes available.

1. Make sure the FIP diagnosis is correct

No matter how good the treatment is, if the cat does not have FIP, then FIP treatment won't work. This sounds very obvious, but you'd be surprised how often the diagnosis is wrong. A negative FCoV antibody test (performed on blood, not effusion) rules out FIP in the vast majority of cases, provided the test is sensitive enough.

If the cat hasn't begun to improve with GS-441524 treatment within one week, then recheck the diagnosis and make sure that there isn't a second condition afflicting the patient: see item number 7. I'm not saying the cat will recover in a week, but there should be significant signs of recovery beginning, e.g. resolution of effusion, increase in appetite.

FIP diagnosis in a nutshell

A negative FCoV antibody test <u>on a blood sample</u> (not effusion) rules out FIP in all but very rare cases, but make sure you use a sensitive antibody test such as the Biogal FCoV Immunocomb. Addie et al, 2015

You can feel reasonably certain that the FIP diagnosis is correct if you have:

- A positive FCoV RT-PCR test on an effusion (effusive FIP) or fine needle aspirate of a mesenteric lymph node or other organ (for non-effusive FIP) is diagnostic of FIP in all but very rare cases.
- Histopathological confirmation of FIP on a biopsy.

If FCoV RT-PCR testing is not available, or you think the test gave a false negative result, then please follow the steps of the FIP Diagnostic Algorithm from www.catvirus.com downloads page (available in several languages) to form an educated opinion. Do NOT use FCoV RT-PCR tests on blood samples because of the high rate of false negative results.

Please watch these films:

Why did GS-441524 not cure this cat?

Bitchute: https://www.bitchute.com/video/ieNrleJ2KJeo/

YouTube: https://youtu.be/KmB6lu8Jg2Q

Rumble: https://rumble.com/v13riqd-why-did-gs-441524-not-cure-this-cat.html

Odysee: https://odysee.com/@Catvirus:3/Theo ascitic cat:f

My cat has FIP:

https://youtu.be/dDIHYKAnDuY

Does Pancho Have FIP?

https://www.youtube.com/watch?v= JLdLQKpoyA

Does Tommy Have FIP? (Parts 1-5) can be found on these platforms:

https://youtu.be/F_rRr6pZ1RE

https://www.bitchute.com/video/z06chepJrPZ5/

https://odysee.com/@Catvirus:3/FelineInfectiousPeritonitisTommy1:a

 $\underline{https://brandnewtube.com/watch/does-tommy-have-dry-feline-infectious-}\\$

peritonitis bsaDjmSe5lSxw8i.html

2. DO NOT USE CORTICOSTEROIDS

Corticosteroids will sabotage the treatment and should only be used palliatively when all hope is lost. Continued use of corticosteroids in a cat you are treating for FIP will predispose the cat to a relapse: if an anti-inflammatory is absolutely necessary use meloxicam instead (following a suitable wash-out period, of course).

3. USE AN ORAL FORM OF GS-441524, NOT GS INJECTIONS AND NOT REMDESIVIR

I am increasingly seeing FIP relapse cases in my online consulting practice: most have one thing in common and that is that their treatments BEGAN with an injectable form of adenosine nuclease inhibitor (GS-441524), or was entirely by injection. The remainder were also given corticosteroids along with the antiviral.

FCoV replicates in the intestine and the oral antiviral hits it at the site of greatest replication. In contrast the injections have poor penetration of the intestine, therefore drug-resistant escape mutants are more likely to appear, often crossing the blood brain barrier, leading to neurological relapses.

I will update this article once I have a film to illustrate this point. I will also update it when I figure out how best to cure these unfortunate cats. At present, we are using the following:

- Oral GS-441524 (e.g. from Bova Specials, UK, Ltd) at neurological doses (i.e. 20mg/kg Bova GS-441524 which is the equivalent of one Mutian 200 per kg) q24h in divided doses with food (to slow passage through the intestine and increase absorption) for 12 weeks. EIDD (molnupiravir) can be used alongside GS-441524 to increase the chances of halting viral replication in the brain.
- o Meloxicam, provided blood pressure and kidney function are normal.
- o Gabapentin.
- o 100,000 units of Virbagen Omega (feline interferon) by mouth q24hrs.
- o Calcitriol 9 ng/kg every 3-4 days (twice per week). Stop if blood calcium increases.

4. TEST FAECES FOR FCOV RNA BEFORE STARTING TREATMENT AND ONE WEEK INTO TREATMENT TO CONFIRM THAT THE DRUG WORKS

This gives us a useful non-invasive method of testing whether the drug you are using is effective against the virus that the cat is infected with, or whether the virus is resistant to the drug. However, only 75% of cats with FIP shed virus in their faeces.

Take a faecal sample (without cat litter, which can inhibit the RT-PCR reaction) <u>before</u> beginning the antiviral drug to ensure that the cat is shedding virus because remember that around 25% of cats with FIP no longer shed virus, so you can't just assume that the cat is shedding FCoV.

Test the faeces again one week into the antiviral drug course by FCoV RT-PCR test: if the drug is working, the faeces should have become negative, or at least the C_T should have increased significantly indicating reduced virus load. If the sample is still positive then your antiviral is not working against the virus infecting the cat and you need to use another type of antiviral: antivirals are either nucleoside analogues (e.g. GS-441524, molnupiravir) or 3C-like protease inhibitors (e.g. GC376).

5. GIVE A 10 DAY COURSE OF DOUBLE DOSE ANTIVIRAL DRUG TO CLEAR THE BRAIN OF VIRUS

Antiviral drugs do not cross the blood-brain barrier well; therefore double doses of nucleoside analogue antivirals are used in neurological cases. In an attempt to avert neurological relapses, all my FIP cases are advised to give a short double course of antiviral drug for about 10-14 days, which is best given at the start of the antiviral treatment course. (Obviously neurological FIP cases require treatment for longer than 10 days).

Dose: A double dose of Bova oral GS-441524 equates to 20mg/kg q24 hours in divided doses. The double dose for Mutian is one Mutian 200mg per kg q24 hours in divided doses. I'm sorry I don't know the doses for Spark, Aura Lucky, Pine, Hero or other brands, but Pedersen & Jacque wrote an interesting article called "Treatment with oral formulations of GS-441524" which does have dose rates for many brands.

Pills should be followed by food to slow transit through the GI tract to facilitate maximum systemic absorption, and of course to prevent oesophagitis.

After 10 days, you can reduce to normal dose except in intra-ocular or neurological cases, which will have to remain on the higher dose until recovery from clinical signs.

6. REMEMBER TO INCREASE THE DOSE OF THE ANTIVIRAL DRUG AS THE CAT GAINS WEIGHT

Giving too little of the drug could cause the virus to become resistant to the antiviral drug, therefore it's important to monitor the patient's weight weekly and adjust the dosage accordingly. Cats recovering from FIP gain weight remarkably quickly: about 25 grams (one ounce) per day on average.

7. Don't mistake concurrent disease for treatment failure

About 50% of cats with FIP are lymphopenic; therefore their immune system isn't functioning well which makes them prone to secondary diseases. The most common of these are infectious anaemia (haemotropic Mycoplasmosis, formerly known as *Haemobartonella felis*), toxoplasmosis and recrudescence of latent feline herpesvirus infection. Bizarrely, cats with FIP also seemed to be prone to trichobezoar, which is why I recommend giving a soup spoon of Royal Canin 12+ Ageing dry cat food to all FIP patients, regardless of their age: in my personal experience that food is the best for reducing furballs.

It is important to accurately diagnose any secondary condition and treat accordingly, rather than jump to the conclusion that your FIP treatment isn't working. If you have done the preparatory work outlined in Paragraph 4 above, you will know whether or not the antiviral you have chosen is able to eliminate the virus infecting your patient.

8. TREAT WITH ANTIVIRAL DRUG UNTIL TWO CONSECUTIVE NORMAL AGP TESTS

A relapse is more likely to occur if FIP treatment is stopped too soon, so it's important to know for certain when a cat is cured, rather than in remission, and simply treating for 12 weeks does not guarantee that a relapse will not occur.

A normal alpha-1 acid glycoprotein (AGP) level rules out a diagnosis of FIP.* Raised AGP is a useful diagnostic marker for FIP: it is sensitive, but not specific. Giori et al, 2011 A consistent reduction of AGP to normal levels was shown to be an indicator of recovery from FIP Addie et

NOTE: on rare occasions, cats with neurological FIP do not have raised AGP.

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^{al, 2022} whereas cats who were only in remission tended to have raised AGP levels, despite whatever treatment they were on.

We test AGP levels at about 3-4 weeks into treatment to see if it has reduced, if it is still raised, we re-test 7-14 days later. Once we have two consecutive normal AGP results (≤500µl) at least one week apart we stop the GS-441524 treatment and go on to oral Virbagen Omega (see below).

A consistent reduction in serum amyloid A (SAA) levels may also work: we know it is raised in FIP, Giordano et al, 2004 and that it reduces with Mutian X treatment, Krentz et al, 2021 but nobody has yet published whether or not it is a marker for differentiating FIP recovery from remission.

The average time that cats required oral GS-441524 (Mutian X) treatment was 7-8 weeks, but some cats did require longer courses. I don't know how long treatment with other brands takes to effect recovery: most vets estimate 12 weeks, based on the Pedersen study Pedersen et al, 2019 but really scientific studies are required to establish protocols based on evidence. My belief is that a one size fits all treatment is not going to work for FIP and that an optimal treatment regime is required for each cat as an individual.

9. ELIMINATE FCOV FROM IN CONTACT CATS TO PREVENT RE-INFECTION OF THE PATIENT

OK—so re-infection isn't a relapse, and in truth, we don't know if a re-infected cat would experience an FIP relapse or not, but why take that chance? Therefore to avoid re-infection of the patient we test the faeces of other cats in the household to find out which of them is shedding FCoV. Cats which shed virus get a 5-7 day course of oral GS-441524 (on an empty stomach, to enable the drug to reach the colon, where the virus is, but followed by a small amount of food or liquid) and their faeces were tested afterwards to make sure they were no longer shedding virus.

So far this protocol has prevented FIP in those cats, which is an added bonus. Another unexpected and welcome result was that the guardians of 5 of 85 cats told us that their cats' chronic diarrhoea problems resolved after the short oral GS-441524 course.

Film of a cat with chronic diarrhoea who recovered after FCoV was eliminated:

Bitchute: https://www.bitchute.com/video/Rt1e8hhrgOMW/

Rumble: https://rumble.com/vrlrbh-feline-coronavirus-chronic-enteritis-and-faecal-

incontinence.html

Brighteon: https://www.brighteon.com/ffd6bc5a-8013-4ac5-bb01-5fe86c98abc9

Odysee: https://odysee.com/@Catvirus:3/Feline coronavirus enteritis:b

Bastyon:

https://bastyon.com/index?v=47610de929e97f57e34fb45990036792a4926f13d7325a2fa5405a78de f37bc7

(This film was not put onto YouTube because of YouTube censorship: I did not want to risk my channel being obliterated. I also want to support the new freedom of speech platforms which are springing up.)

10. FOLLOW UP THE ANTI-VIRAL TREATMENT WITH 100,000 UNITS OF VIRBAGEN OMEGA (VO) BY MOUTH PER CAT Q24H ...

... (or zinc picolinate and 10mg/kg mefloquine (Lariam, Roche) 2 or 3 times per week if VO not available)

I was using feline interferon omega (Virbagen Omega, Virbac, France) along with meloxicam to treat FIP before the antivirals were discovered, and I now recommended that it be given at a low dose after the antiviral course as a kind of safety net. My recommendation is 100,000 units per cat by mouth every day: one vial usually lasts about 3 months. The dilution instructions can be downloaded here: www.catvirus.com/treatment.htm#Virbagen

My recommendation is to continue this until the cat's FCoV antibody titre falls significantly (i.e. over three-fold) which is evidence that there is no more virus in the body stimulating an immune response.

I have to admit to not being absolutely sure that this step is necessary, but none of my patients who got this aftercare relapsed, whereas I was referred a case that was treated elsewhere for 12 weeks with GS-441524 but did not get feline interferon and relapsed.

If Virbagen Omega is not available, an alternative is zinc picolinate (5mg/cat q24h) and mefloquine (Lariam, Roche) at 10mg/kg every three days.

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