An update on treatment of FIP using antiviral drugs in 2024: growing experience but more to learn

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The above specialists run the 'FIP advice' email address (fipadvice@gmail.com) for vets, answering queries on the new treatments on a voluntary basis and disseminating information to veterinary professionals around the world. So far, they have answered nearly 2000 emails via this free service, hoping this increases access to care for FIP in cats.

Introduction

In the UK antivirals with high efficacy in the treatment FIP have been legally available since 2021 (initially remdesivir, and subsequently its active form GS-441524). In that time, we have gained experience in managing the disease and monitoring treatment, and seen excellent outcomes. Legally available sources of antivirals now exist in many other countries, although in some parts of the world there remains no quality assured, legal supply. This article summarises the current advice on treatment of FIP to aid practitioners managing these cases and is based on current information that may change as more experience and publications become available. It includes information on the recently available additional antiviral EIDD-1931 (the active form of molnupiravir). Treatment needs to be tailored to the individual cat based on response, compliance, and client finances. For further information on making a diagnosis of FIP please see further reading below and the ABCD FIP diagnostic tool flow diagrams here: https://www.abcdcatsvets.org/portfolio-item/factsheets-tools-for-feline-infectious-peritonitis-fip/.

Treatment protocols (updated February 2024)

Legally available antivirals in the UK and other countries via import now include remdesivir (injectable), GS-441524 (oral suspension and oral tablets), and EIDD-1931 (oral tablets). The following advice is based on published and unpublished data and experience. Treatment of individual cases remains the responsibility of the attending veterinary surgeon. The dosages below are based on experience using reputable preparations of known antiviral content. Extrapolation is not applicable to other oral preparations where the active component and/or its content are not known or provided by the manufacturer.

Use of oral GS-441524 for the whole treatment course, including at the start

Oral GS-441524 (available as a suspension of 50 mg/ml and tablets of 50 mg tablet or 25 mg (half a 50 mg tablet)) can be used from the start of FIP treatment for the entire (e.g., 12-week/84-days) course. It is important to support owners in medicating their cats, which can be challenging. Oral GS-441524 suspension or tablets can be given with a small treat (tablets can be crushed for this) or directly into the cat's mouth. Further study is needed to review the effect of food on absorption, but it is recommended to give in a small treat or on an empty stomach, leaving a gap of an hour or more before feeding a larger meal.

Fasting cats overnight can increase their hunger to facilitate medicating in the morning, and similarly for an evening dose. However, starving kittens is never recommended as they cannot cope with this. Any withholding of food needs to be tailored to the age of the cat.

Injectable remdesivir is reserved for cats that cannot be medicated orally

Injectable remdesivir (10 mg/ml) is effective in the treatment of FIP but is associated with some side effects (see below), particularly pain on subcutaneous injection which is seen in 50% of cats. Previous FIP treatment protocols suggested this be used at the start of treatment before transitioning to oral GS-441254. However, we now know that FIP cats can be treated successfully with oral GS-441524 from their first day of treatment. This avoids pain on injections and reduces the costs of the treatment (the dose for the weight of the cat using GS-441524 is cheaper than remdesivir). Use of injectable remdesivir should be reserved for the following situations:

- Severe neurological signs and inability to swallow or tolerate oral medication;
- Extremely dehydrated/unwell cats;
- Cats that cannot be orally medicated for other reasons.

In some circumstances, if a cat is hospitalised and has a poor appetite, which is affecting the ability to medicate it, 48 hours of remdesivir (given intravenously not subcutaneously) can result in significant clinical improvements which may facilitate subsequent oral medication with GS-441524. The remainder of the treatment course can then be given as an oral GS-441524.

Duration of antiviral treatment is still a minimum of 84-days

The current recommendation is to treat for 84-days minimum. Some cats have been successfully treated with shorter courses, but large case studies have not yet been published. If cost constraints necessitate shorter courses, the dosage used should not be reduced and treatment sustained for as long as possible.

The transition between remdesivir and oral GS-441524 can be immediate, i.e., from one treatment to the next.

Dosage recommendations

With experience, and as yet unpublished data on therapeutic drug monitoring (TDM), dosage recommendations have increased from previous FIP treatment protocols. However, evidence shows that over 85% of cats respond to the previously recommended drug dosages, which is still high. However, based on TDM studies, we now know that individual cats vary in their absorption of oral GS-441524, with those absorbing poorly requiring higher dosages to achieve clinical and biochemical remission. Ideally, dosage should be adjusted based on TDM, if available (see below), or response to treatment.

Compared to previous FIP treatment protocols, the important changes to dosage recommendations are:

- Dosage of oral GS-441524 given as a divided dose, twice a day (every 12 hours), to optimise serum levels of GS-441524;
- Higher dosages may overcome issues with poor absorption in some cats and have a better chance of crossing the blood brain barrier and the blood eye barrier;
- Dosage should be adjusted according to response, and TDM if available.

Table 1

Clinical presentation	GS-441524 PO dosage	Remdesivir IV or SQ injection dosage
Effusion(s) and without ocular or neurological signs	6.0 – 7.5 mg/kg q 12 hours (i.e., 12 – 15 mg/kg/day given as a divided dose q 12 hours	10 mg/kg q 24 hours
No effusion and without ocular or neurological signs	6.0 – 7.5 mg/kg q 12 hours	12 mg/kg q 24 hours
Ocular signs present (± effusion)	7.5 – 10.0 mg/kg q 12 hours	15 mg/kg q 24 hours
Neurological signs present (± effusion)	10 mg/kg q 12 hours	20 mg/kg q 24 hours

PO, per os (orally); IV, intravenous; SQ, subcutaneous; q, every; hours

Cats should be re-examined after 1-2 weeks (sooner if not improving or deteriorating) and dosage adjusted depending on monitoring at this point (see 'Monitoring').

Notes on weighing cats

It is very important to weigh cats weekly during treatment, using accurate scales e.g., cat or baby scales. Weight gain and/or growth in kittens will occur with successful treatment necessitating an increase in dose to ensure that the dosage of antiviral administered is still appropriate for the type of FIP being treated as in Table 1.

Not increasing the dose as the kitten grown appears to be one of the most common causes for a poor response to treatment, and treatment failure.

Therapeutic drug monitoring (TDM) of oral GS-441524 during treatment

TDM is available currently at Edinburgh University. Cats are sampled after 3-5 doses of starting the oral GS-441524; ideally, 2-3 ml serum and 0.5 ml EDTA should be taken at peak (2-3 hours post-dose) or trough (9-12 hours post-dose) times after GS-441524 is given. This can be combined with alpha-1 acid glycoprotein (AGP) measurement. 1.5 ml serum is the minimum volume required for TDM and AGP measurements without haematology and biochemistry testing. Email Rachael Hammond (Rachael.Hammond@ed.ac.uk) for information on submission. Results can allow adjustment of GS-441524 dosage or frequency of administration. TDM measurement is currently (February 2024) available free of charge.

What to expect during treatment

- In the first 2-5 days you should see an improvement in demeanour, appetite, resolution of pyrexia, and reduction in abdominal or pleural fluid (if present).
- NB. More clinical signs attributable to FIP may be seen during the initial few days of treatment, i.e., before the medication has had time to take effect. This can include the development or recurrence of pleural fluid which may require drainage (if the cat is at home, advise the owner to measure resting respiratory rate and effort). Neurological or uveitis

signs may also develop (e.g., owners may notice a change in iris colour). If neurological or ocular changes are noted, the drug dosage should be reviewed in case an increase is indicated.

- Effusions usually resolve by 2 weeks. If an effusion is still present at 2 weeks, consider increasing dosage (by 2-3 mg/mg twice daily (every 12 hours) if possible) e.g., increasing the dosage to above that used for cats with effusions only.
- Serum albumin increases and globulin decreases (i.e., they normalise) may take several weeks, but note that globulins can initially increase when a large volume effusion is absorbed. In some cases, globulins may remain mildly increased even at the end of the treatment course and this has not been associated with relapse if all other parameters have normalised.
- Lymphopenia and anaemia may take longer to resolve, up to 10 weeks, and a lymphocytosis (and eosinophilia) can occur during successful treatment.
- Enlarged lymph nodes typically reduce in size over a few weeks but in some cases, they do not return to normal size nor normal ultrasonographic echogenicity, even by the end of treatment. However, this does not seem to signify FIP relapse, if all other parameters have returned to normal; treatment can be stopped as planned and the patient monitored.
- If progress is not as expected, consider reviewing the diagnosis (see below) and/or increasing the dosage.

Prognosis

Response rates are around 85%, with cats that respond rapidly (e.g., returning to completely normal within 30 days) having a better overall response. Some cats fail to respond to antiviral treatment, often deteriorating in the first 2 weeks; some cats may be too sick for the antivirals to work (although consider intravenous remdesivir in sick cats that cannot be medicated otherwise). Relapse is uncommon (<10%) but tends to occur in the first few weeks after stopping treatment. Using TDM to inform dosing, and/or higher dosages, may result in higher response rates. Survival times are long (although we are all still learning about this) with late relapses (or reinfections) rarely reported. Since the drugs have only been available since late 2021, we don't yet know if cats that appear to be cured stay that way lifelong, although results so far are very encouraging.

Note on using antiviral treatment trials as an aid to diagnosis

In some situations, it is not possible to achieve a definitive diagnosis of FIP due to cost constraints, availability of testing, or instability of the patient precluding invasive testing. Antiviral treatment trials can be considered using an appropriate dosage and objective measures to identify improvement e.g., serial neurological or ocular examinations. Improvements in demeanour and return of normothermia are expected within 48 hours, and add weight to the diagnosis. Note that effusions can take longer to resolve (see 'What to expect during treatment') and improvements in haematology and biochemistry abnormalities can also take weeks. Failure to improve on an adequate dosage of antivirals (preferably with TDM if available) should prompt investigation for an alternative diagnosis. Most cats are notably better by 2-5 days, however, a small number of cats can take up to 10 days; however, there have usually been some positive signs before then.

Monitoring during treatment

Clinical response is most important to monitor; a failure to improve may necessitate an increase in dosage. Monitoring should be adequate to assess response but, particularly when the cat is doing well, repetition of costly tests that are unlikely to alter treatment (e.g., limiting testing to previously abnormal parameters and basic screen) and multiple, potentially stressful, clinic visits should be limited. Owners should be encouraged to weigh their cat at home (e.g., using inexpensive baby scales) and keep a diary of appetite and demeanour, respiratory rate and other parameters as indicated. The recommendations below will change depending on the cat's response to treatment:

- After 48 hours an improvement in demeanour and normothermia is expected. A verbal report of progress and ease of medicating the cat should be obtained around this time.
- After 2 weeks weight, demeanour, effusions (in-house scanning, abdominal girth measurement) should be reviewed. Additionally, serum biochemistry and haematology can be assessed, adapting to cost constraints as needed (e.g., consider whether measurement of total protein, PCV, and plasma colour assessment, using a spun microhaematocrit tube, could be used as a cost-effective and rapid initial screen to indicate whether additional testing is indicated). Normalisation of serum AGP (if elevated before treatment) may be useful to predict remission;
- After 6 weeks the cat should be re-examined and the above assessments repeated.
- After 12 weeks the cat should be examined before stopping treatment and all assessments should ideally be normal. Mild persistent hyperglobulinaemia and mild abdominal lymphadenomegaly are sometimes reported and not associated with relapse. If all other parameters are normal (including AGP) then treatment can still be stopped.

Point-of-care ultrasonography (POCUS) to monitor for effusion resolution and/or lymph node size is useful if available and affordable.

Monitoring after treatment

Once treatment is completed (usually 12 weeks' duration), cats should be monitored for relapse by their owners; loss of appetite, weight changes, or other clinical signs. The clinical signs of relapse may differ from those at initial diagnosis (e.g., neurological signs in cats that previously had effusions). Ideally, the cat is examined ~4 weeks after stopping treatment. Monitoring AGP may provide reassurance if it remains normal. Any clinical signs should be promptly investigated.

Supportive care for FIP cats

Cats with FIP may benefit from various types of supportive care. No specific supplements have been studied alongside antivirals, and multiple oral medications may not be optimal due to compliance (as well as additional costs). However, sick and dehydrated cats may require intravenous fluid therapy. The following interventions can be considered depending on the case:

- Affected cats may be painful e.g., from pleural and peritoneal inflammation, distension from masses, uveitis, and neurological lesions. Treatment with opioids, such as buprenorphine, may be of benefit and other drugs such as NSAIDs (if hydration status and renal parameters are normal and the cat is eating) as part of multimodal analgesia;
- Repeat drainage of pleural effusions may be required during the initial treatment period. Abdominal effusions are not normally drained, unless they are causing respiratory compromise due to pressure;
- Cats with FIP have often lost weight and body condition so nutrition is a priority. Appetite stimulants such as mirtazapine (and/or capromorelin oral solution) may be useful and some sick cats benefit from feeding tube placement short-term, which can facilitate medicating; since nasal tubes are poorly tolerated by cats and may cause depression, cats with profound anorexia that cannot be alleviated by the drugs above may benefit from an oesophagostomy (O-)tube being placed;
- Drugs such as maropitant may benefit cats feeling nauseous and encourage eating;
- Occasionally, FIP can cause severe (sometimes haemolytic) anaemia and blood transfusion can be considered alongside antivirals;
- Hepatoprotectants e.g., S-adenosyl methionine (SAME), with or without silybin are not usually required, even in cats with ALT enzyme activity increases;
- Generally, corticosteroids are contraindicated in the treatment of FIP with antivirals to avoid adverse effects and immunosuppression. However, cats with uveitis may need topical corticosteroids and cats with severe neurological signs occasionally require short-term systemic corticosteroids (1-5 days) to reduce inflammation. Rarely, cats with FIP develop immune-mediated haemolytic anaemia (IMHA) and these often require systemic corticosteroid treatment for more than a few days to help resolve the anaemia alongside the antiviral treatment. If an anti-inflammatory agent is required in cats undergoing FIP treatment, consider using an NSAID (if hydration status and renal parameters are normal and the cat is eating).

In the event of a poor response during treatment or relapse

e.g., recurrence or lack of resolution of effusion, pyrexia, development of new ocular or neurological signs, or persistent clinical pathology abnormalities:

- Ensure that you are still confident that the cat has FIP; review the diagnosis, look for additional pathology, and consider repeat sampling (e.g., external laboratory analysis and culture of any fluid; cytology or biopsy of lymph nodes ± feline coronavirus antigen or RNA detection, but bear-in-mind that finding the virus is more difficult when on treatment), AGP;
- Consider TDM if available to check serum GS-441524 levels to inform dosing;
- If relapse occurs during treatment; increase the dosage of GS-441524 (or remdesivir) by 2-3 mg/kg per dose and monitor as above, ensuring treatment is not stopped before the cat has been normal clinically and on clinical pathology for at least 2 weeks. The increased dosage used will depend on the dosage the cat is on at the time of the relapse, the nature of the relapse and finances, but can be

up to that recommended for neurological FIP (see dosage table above) or even higher (please seek guidance when considering this);

- If relapse occurs after completion of treatment; restart GS-441524 (or remdesivir) course at a higher dosage (minimum 2-3 mg/kg per dose higher than used previously) and ideally treat for another 12 weeks. The increased dosage used will depend on the dosage the cat was on before its relapse and the nature of the relapse, but can be up to that recommended for neurological FIP (see dosage table above);
- If the cat is already receiving a high dosage of GS-441524 and/or TDM serum levels are adequate, consider switching to EIDD-1931 (see below) and seeking guidance (FIP advice email or specialists), as adjunct treatments such as mefloquine, feline interferon or polyprenyl immunostimulant may be options (see below).

EIDD-1931

This drug is another antiviral effective for the treatment of FIP in cats, although knowledge of its usage is much less than for GS-441524. The recommended dosage is 15 mg/kg every 12 hours, and it is available in 60 mg tablets for oral use. Potential adverse effects include cytopenia, especially neutropenia, rarely pancytopenia, reduced appetite/nausea, increased ALT enzyme activity and, potentially, renal compromise. Use of EIDD-1931 should be reserved for:

- Cats failing to respond to treatment with GS-441524 or remdesivir despite adequate dosage (ideally assessed with TDM);
- Cats relapsing after treatment with GS-441524 or remdesivir at adequate dosages.

Neutering, parasiticide treatment, and vaccination during or after treatment for FIP

- Neutering is ideally performed from a month after treatment is completed if the cat has responded well. However, if leaving the cat unneutered is causing stress e.g., attempts to escape or distress when queens are on heat, neutering during therapy may be preferred, ideally when the cat is doing well on treatment with at least another 4 weeks of treatment remaining. Some measure AGP to confirm it is normal before neutering;
- There is no contraindication to routine worming and flea treatment for cats on GS-441524 or remdesivir;
- No information is available on response to vaccination of cats receiving treatment for FIP although analysis of treated cases suggests that cats can be safely vaccinated after or during successful treatment without causing relapse. Vaccines should be administered as is normally recommended for the cat depending on its environment and risk (see WSAVA or ABCD Vaccination Guidelines). If urgent vaccination is required whilst the cat is being treated, due to the risk of infectious disease, vaccines can be given if the cat is well;
- If veterinary visits and procedures are necessary, clinic stays should be minimised, and Cat Friendly Clinic protocols and handling implemented to reduce stress to the cat.

Treatment with feline interferon (IFN), polyprenyl immunostimulant, or mefloquine

- Combinations of IFN omega, polyprenyl immunostimulant, and mefloquine have been used in the period following the end of treatment with GS-441524 (or remdesivir) in some cats; however, currently there is no evidence to suggest they are needed as high response rates of over 85% have been seen without these adjunct treatments;
- Mefloquine has also been used to treat cats with FIP when cost constraints absolutely prohibit the use of a full course of, or increased dosage of, more effective antivirals such as GS-441524. Studies are needed to evaluate its effectiveness but it should only be used when absolutely no alternatives are available as GS-441524 is known to be very effective.

Further reading

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