Treatment of FIP in cats with Remdesivir

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Until recently, a diagnosis of FIP was a death sentence for a feline patient. Although omega-interferon and polyprenyl immunostimulant had reasonable efficacy in some cases, most cats and kittens diagnosed with FIP died or required euthanasia on welfare grounds.

That all changed a few years ago because of the culmination of lifelong FIP research by Professor Niels C. Pedersen at UC Davis. Niels first showed a purpose designed protease inhibitor GC-376[1,2] could save the lives of some cats with FIP, and soon thereafter he showed that the nucleoside analogue GS-441524[3,4] was even more effective for treating FIP, although the dose required depended on whether there was ocular or CNS involvement.[5] GS-441524 was a drug developed by the US company Gilead, which disappointingly, has shown no interest in developing the molecule as a veterinary treatment for FIP. So, to fill in the void for effective FIP therapy, various companies started making GS-441524 and selling it as a black-market drug. Although it was very expensive, the widespread availability of good quality GS-441524 provided a way for dedicated cat owners to save cats with wet or dry FIP, although procuring the drug was complicated, usually relying on the help of a Facebook collective. Unfortunately for cat lovers, the APVMA and Australian Veterinary Practitioner Boards eventually twigged to what was happening, and Border Force made it more difficult to source GS-441524 and safely import it for veterinary use, with punitive threats to veterinarians who facilitated the treatment of cats with FIP.

Ironically, the COVID 19 pandemic provided a solution to this problem. Gilead had developed Remdesivir (GS-5734) as a drug for treating human Coronavirus disease, and this drug was given provisional registration by the TGA in June 2020 for treatment of SARS-Cov-2 infections in human patients. This process would normally have taken several years, but COVID expedited the process. Remdesivir is essentially GS-441524 with some extra phosphate groups added to improve intracellular penetration (Figure 1B). As Remdesivir was a licensed human drug, it can be readily used off-label in veterinary applications, such as treatment of FIP in cats and kittens. This circumvented problems with using an unlicensed drug purchased on the black market, with the allied issues of unproven efficacy, purity, and consistency.

BOVA Aus has managed to secure a reliable source of Remdesivir to formulate. Studies in Australia have determined the shelf-life and confirmed efficacy *in vitro* against Coronaviruses. For the past 6 weeks we have been using it in clinical cases of FIP in cats and kittens. Some of these cases have been new diagnoses, while others were cats that had already improved with black-market-sourced GS-441524 that had subsequently become unobtainable. There was a mixture of effusive and non-effusive cases. Based on a small number of cats, Remdesivir seems to be highly effective at managing FIP infections. It is slightly easier to administer than the parent drug and seems a little less painful following subcutaneous administration. It is provided in a 100 mg vial which is reconstituted with 9 mL of sterile water for injection to give a 10 mg/mL solution (10 mL per vial after reconstitution).

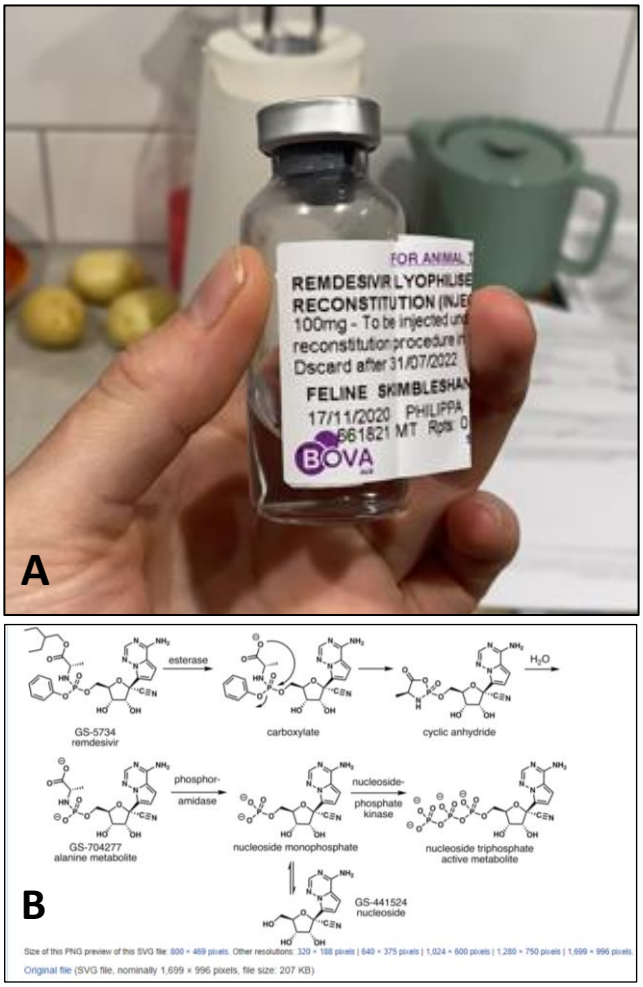

Figure 1. (A) BOVA Remdesivir reconstituted and ready for therapy. (B) The pathway by which Remdesivir travels intracellularly to be activated as GS-441524

In newly diagnosed cats with severe disease, we have chosen to place the cats on intravenous fluid therapy for the first 3 days of therapy, and administer Remdesivir at a high dose (10 mg/kg diluted to 10 mL with saline and given over 10 minutes) intravenously to provide a loading dose, thereby achieving rapid antiviral efficacy; cats clinical signs have improved markedly over 2-3 days during preliminary therapy. Cats are then transitioned to subcutaneous therapy, usually at a lower dose. For routine FIP cases – we generally have used 5-6 mg/kg once daily (SIUD) as

Remdesivir is thought to be roughly equipotent to GS-441524 (Niels Pedersen, personal communication). If there is prominent ocular involvement, we recommend 8 mg/kg SID and cats with neurological FIP with CNS signs are given 10 mg/kg SID.[5] Treatment is then continued using daily subcutaneous injections for 2-3 months. In cats that find the SC injections painful, we have used gabapentin and/or buprenorphine for sedation/analgesia, and in some cases placed a new cephalic catheter every 5 days to allow owners to give IV therapy rather than SC injections. In situations when owners cannot afford a full course of therapy, or where injections are deemed to be too painful, we have used mefloquine (62.5 mg 2-3 times a week; obtained from BOVA or a local pharmacy) after preliminary Remdesivir therapy for its antiviral effect based on the work of Jacqui Norris and colleagues at the University of Sydney.[6]

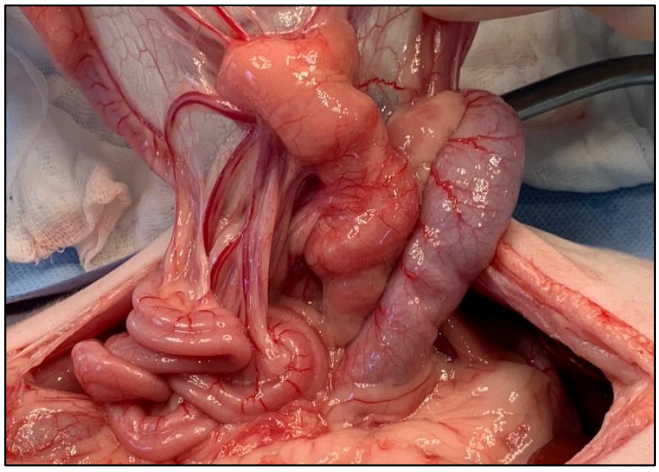

Figure 2. Focal dry FIP, with pyogranulomatous inflammation of intraabdominal lymph nodes. Rather than undertaking an exploratory laparotomy, lymph node biopsy, histology and immunohistology, it might be more cost effective to trial 3 days of IV Remdesivir therapy.

The main advantage of Remdesivir therapy for FIP is that the active we are using is present in an approved drug for human use. It is only a matter of writing a prescription with the client's name and address, the name of the patient and the dose to be administered, and BOVA can usually compound and provide vials to any veterinarian in Australia within 24-48 hours. Currently, the cost of a 100 mg vial is $250 plus GST and postage, although it is possible that in time the cost will come down because of economies of scale. We believe most owners will feel much more comfortable obtaining a product from a well-known Australian company, rather than sending money overseas and hoping that black-market drugs will make it to Australia safely from China.

Veterinarians wishing to explore this option, or with general questions about FIP, can e-mail Richard Malik (richard.malik@sydney.edu.au) for advice in relation to diagnosis or therapy. The diagnosis of FIP is beyond the scope of this newsletter, but cats with effusive disease are most easily diagnosed by cytology and fluid analysis of body cavity effusions, with subsequent immunohistochemistry performed at VPDS, University of Sydney (easily arranged through Vetnostics, QML, ASAP, VetPath, Gribbles or IDEXX). Dry FIP is more problematic, as usually it requires a fine needle aspirate biopsy of pyogranulomatous lesions in the liver, kidney, or abdominal lymph nodes. **We have found that 3 days of IV Remdesivir therapy can be used as a cost effective therapeutic trial in cats with dry FIP as an alternative to biopsying intra-abdominal structures at exploratory laparotomy, as in FIP cases there is a prompt improvement in most clinical signs.** If veterinarians are uncomfortable managing FIP cases with Remdesivir themselves, we can provide a list of veterinarians with a special interest in treating FIP who would be happy to accept such cases as referrals.

Figure 3. Which cat has FIP and is being treated with Remdesivir?

References

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