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Literature review and questionnaire-based retrospective study: The Treatment of Neurological and Ocular Feline Infectious Peritonitis with The Nucleoside Analogue GS-441524

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List of abbreviations

- FIPV- Feline Infectious Peritonitis Virus
- FIP- Feline Infectious Peritonitis
- FCOV- Feline Coronavirus
- FeCOV- Feline Enteric Coronavirus
- CaCoV- Canine Coronavirus
- TGEV- Transmissible Gastroenteritis Virus
- SPF- specific pathogen free
- CNS- Central nervous system (brain, spinal cord)
- FeLV- Feline Leukaemia Virus
- BBB- Blood brain barrier
- A:G- Albumin to globulin ratio
- CBC- complete blood count
- WBC- white blood cells
- BUN- blood urea nitrogen
- ALT- alanine transaminase
- MRI- magnetic resonance imaging
- RT-PCR- real time polymerase chain reaction
- PCR- polymerase chain reaction
- CBC- complete blood count
- CT- computed tomography
- MRI- Magnetic Resonance Imaging

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Introduction

Feline Infectious Peritonitis (FIP) is a viral illness stemming from the Alphacoronavirus genus. This severe ailment in felines results from a virulent mutation of the Feline Enteric Coronavirus (FCoV). FCoV is a widespread virus that affects cats across the globe, usually causing no harm and sometimes providing immunity. However, in certain cases, it mutates into FIPV (FIP virus), which is a highly aggressive and often fatal form. Once infected with FIPV, the virus replicates in white blood cells, leading to widespread inflammation and damage to various organs. FIP has two main forms: wet and dry. Less common variants of FIP include neurological and ocular forms. Neurological FIP involves brain and spinal cord inflammation, leading to symptoms such as seizures and tremors. Ocular FIP is characterized by eye inflammation, which can cause cloudiness, redness, and, in severe cases, blindness.

Diagnosing this disease remains challenging, as current diagnostic methods do not permit a direct FIP diagnosis. Moreover, there are no licensed veterinary pharmaceuticals available on the market for its treatment. Until recently, FIP was considered incurable, with treatment limited to managing symptoms. However, an antiviral drug called GS-441524 (GS) has shown promise. It inhibits virus replication and effectively treats both wet and dry FIP, including neurological and ocular forms. Treatment typically involves a series of injections over weeks, with the duration and dosage adjusted based on disease severity and treatment response. However, the developer, Gilead Sciences, refuses to licence this drug for veterinary use. For this reason, many pet owners chose to obtain this medication, at times resorting to unauthorized means, with the aim of trying to save their beloved animals. but a significant issue is the lack of scientific documentation due to the sourcing of GS-441524 from illicit markets, especially in the less common neurological and ocular forms.

The objective of this thesis is to compile existing scientific studies and data related to GS441524, offering valuable insights to veterinary professionals, the pharmaceutical industry, and FIP cat owners. Additionally, it includes data gathered from a retrospective and prospective study involving veterinarians, cat owners and others who have used this antiviral treatment on cats. In this report, we use the term 'GS-441524', ‘GS’ and ‘GS- like’ to concisely, to allude to numerous unapproved drug formulations asserting to contain this particular compound, despite not being manufactured by Gilead Sciences.

Literature review

Introduction of Feline infectious Peritonitis Virus (FIPV)

Feline Enteric Coronavirus (FECoV) is classified within the Alphacoronavirus genus of the Coronavirinae subfamily, which belongs to the Coronaviridae family. In 1963, Holzworth initially described the condition as ‘Chronic Fibrinous Peritonitis’ at the Angell Memorial Animal Hospital, Boston. However, it is currently defined by varying levels of systemic serositis, vasculitis, and disseminated pyogranuloma. This virus, possessing a single-stranded RNA genome with a positive-sense and enveloped structure, causes infections in both domestic and wild cats within the Felidae family on a global scale. Based on pathogenicity, feline coronaviruses are categorized into two biotypes commonly known as (FECoV) and feline infectious peritonitis virus (FIPV). Additionally, two serotypes (I and II) host the coexistence of both biotypes. (Desmarets, L., 2015). Serotype I is known to have a higher prevalence in Europe and America, whereas Serotype II has primarily been documented in Asia (G. Tekes, H.-J. Thiel, 2016). Serotype I is known to cause 80-90% of natural infections and is difficult to isolate. Serotype II causes up to 10-20% of infections and is more easily isolated as it replicates in cell culture therefore, it is more commonly studied. Serotype II is the product of a recombination of FeCov and Canine Coronavirus (CaCoV) type II. CaCoV, Transmissible gastroenteritis virus (TGEV), SARS and other human coronaviruses are also known to infect cats and can lead to seropositivity and shedding.

Infection with FECV typically occurs through oral exposure or by inhaling faecal particles from infected cats but it can also be shed in other secretions such as saliva and urine. Queens can also spread the virus trans-placentally. Cats are most commonly infected with this virus when they're about 9 weeks old, and they may get infected multiple times until they are around 3 years old, after which infections become less common. Approximately 20-60% of domestic cats are believed to carry FECV, given the widespread prevalence of this virus in their environment with seropositivity rates as high as 90% in holdings where multiple cats are present (G. Tekes, H.-J. Thiel, 2016).

Coronaviruses are equipped with spike surface proteins, often referred to as 'S' proteins, which facilitate binding to cell receptors throughout the body. This interaction initiates fusion, allowing the virus to enter the cell. Upon entry, viral RNA is liberated into the cytosol of the cell, utilizing the host cell's organelles to orchestrate the production of viral

proteins. Eventually, the virus is released from the cell through exocytosis, enabling its dissemination throughout the body. The primary site of replication for the virus is in the tonsils, lymphoid tissue and apical epithelium of the small intestine, cecum, and proximal colon. Most of these infections are harmless or may result in mild enteritis or diarrhoea. In instances of low virulence infections, no mutations are expected, and clinical recovery with the elimination of the virus typically occurs. Since this enteric infection doesn't establish immune memory, it appears that the cat's immune system remains active due to a consistent but low-level exposure to the virus. This phenomenon clarifies why kittens infected with FECV from their mother may begin to display clinical symptoms as their maternal immunity wanes around 5-6 weeks of age. In contrast, high virulence infections or infections with mutant strains can result in systemic infections, manifesting as FIPV.

In a small percentage of cases (approximately 10%), the virus mutates allowing it to infect macrophages, but in the majority of cases, the infection in macrophages is typically eradicated, except in an exceedingly low proportion (0.3-1.4%) of cats, in which it has the potential to disseminate throughout the body via viraemia associated with macrophages and monocytes. (Pedersen, N.C., 2023).

Viruses belonging to the Coronaviridae family, like numerous other RNA viruses, have a reputation for undergoing frequent mutations during the replication process. Although the precise genetic alteration responsible for heightened pathogenicity remains unidentified, there are studies that show possible trends in the conversion of FeCov to FIPV. Compelling evidence suggests that certain mutations within the spike-protein (S) coding region significantly contribute to this shift (McKay, L.A. et al., 2020). Additionally, there is evidence suggesting that the ORF3c accessory gene may contribute to this transition. *Chang et al's* research revealed that cells lacking expression of the ORF3c-encoded protein could enhance viral replication in macrophages (Chang et al, 2012) Furthermore, another study by *Licitra, B. N et al* proposed that mutations occurring at the S1/S2 cleavage site were observed in FECV cases transitioning to FIPV, thereby promoting viraemia (Licitra, B. N). Thus far, it is understood that these mutations lead to a shift in FECV, causing it to lose its preference for enterocytes while gaining an affinity for monocytes and macrophages. Following their initial presence at disease sites, macrophages proceed to migrate both locally and through the bloodstream. Ultimately, they zero in on the vasculature in the peritoneal cavity, the uveal tract of the eye (including the iris, ciliary body, and choroid), along with the ependyma and meninges in the brain and spinal cord. (Pendersen N.C., 2023)

The degree of FIP severity seems to be primarily influenced by the host's susceptibility and host-specific immune responses, which are often hereditary, with the virus strain playing a secondary role. These events explain why cats exposed to the same viral strain may exhibit a range of lesion severities, spanning from lethal outcomes to asymptomatic cases. Some factors that increase the risk of a cat developing this mutation include being young, having a genetic predisposition, gender, living in overcrowded conditions, poor nutrition, and experiencing stressful events.

FIP clinical presentations and its forms

The clinical manifestations of FIP exhibit variability and are frequently intricate, reflecting differences in the virus and the host's immune response. Roughly 50% of globally diagnosed cats are younger than two years old, and purebred cats tend to be overrepresented. (Norris, J., et al, 2005)

The course of this disease differs in each patient spanning from days, weeks, months to even to up to a year or more in rare cases. The incubation time is complicated to determine but according to studies involving experimentally infected cats that are specific pathogen free (SPF), the incubation period for effusive FIPV is generally 2-14 days long and in non-effusive cases several weeks (G. Tekes, H.-J. Thiel, 2016). The disease can be categorized broadly into two primary forms: wet (effusive) and dry (non-effusive). It's important to note that while there are these two forms, they do not represent entirely distinct entities. A portion of cats may initially exhibit symptoms of dry FIP but subsequently transition to wet FIP throughout different stages of the disease, or conversely. It is commonly observed that around two-thirds of cats will initially show symptoms associated with wet FIP, while the remaining one-third will initially exhibit signs indicative of dry FIP. (Pedersen, N.C.,2023)

Wet or effusive FIP is distinguished by its acute and severe clinical features, characterized by the accumulation of protein-rich serous effusion in both the abdominal and thoracic cavities. This is a result of damages to the blood vessels and vasculitis causing inflammation and leakage of serum into the abdomen and chest. This occurs after a humoral immune response with high antibody production, creating a type III hypersensitivity reaction with vasculitis and is an acute form of FIPV (Myers, A., 2015). This creates the common pot-bellied appearance of FIP cats. Granulomatous lesions such as pyogranulomas can also be found in effusive cases of FIP. This can be seen due to the infected monocytes in the blood

stream abundantly expressing cytokines such as tumour necrosis factor L-1β, and adhesion molecule. This facilitates the interaction between monocytes and endothelial cells in the vasculature. It has also been suggested that the presence of FIPV-infected macrophages and monocytes can potentially elevate vascular permeability due to their production of endothelial growth factor. (G. Tekes, H.-J. Thiel, 2016). In the effusive form of FIP, occurrences of central nervous system (CNS) and ocular involvement are relatively rare.

On the other hand, the dry form is believed to manifest when the cat initiates a combined immune response, with a sufficient T-cell response to restrict the virus to localized macrophage clusters. This is a type IV hypersensitivity reaction and is a chronic form of FIPV. The abdominal lesions noted in dry FIP exhibit distinct characteristics, notably larger size, lower frequency, and more localized distribution in comparison to the lesions identified in wet FIP. In instances of dry FIP, these lesions commonly extend from the pleural and serosal surfaces into the parenchyma. For this reason, it is occasionally denoted as 'parenchymatous FIP'. Dry FIPV is characterized by a reduced prevalence of granulomas found in multiple organs, such as the lungs, liver, kidney, distal intestines and lymph nodes, in both the thoracic and abdominal cavities, and sometimes even affecting the eyes and brain. Notably, involvement of the wall of the colon and caecum, together with caeco-colic lymphadenopathy, indicates a unique subtype within the dry FIP spectrum. This subtype is associated with symptoms characteristic of ulcerative colitis, such as the presence of soft stools containing blood and mucous. (Pedersen, N.C., 2008). While only 9% of wet FIP cases show signs of brain and/or eye involvement, neurological and/or ocular symptoms are the predominant clinical presentations in 70% of cats with dry FIP. (Pedersen, N.C., 2023)

In a study done by UC Davis School of Veterinary Medicine and referred to by Pedersen, C.N., a comparison of clinical signs seen in necropsied cats in both wet FIPV and dry FIPV was undergone. They can be seen in figures 1 and 2 below.

Figure 1. Variability in clinical signs of effusive (wet) FIP

Signs referable to – % affected.

Peritoneal cavity – 58%	Peritoneal cavity, CNS* – 1.9%
Peritoneal & pleural cavity – 22%	Peritoneal and pleural cavity, CNS – 0.9%
Pleural cavity – 11%	Peritoneal and pleural cavity, eyes – 0.9%
Peritoneal cavity, eyes – 2.8%	Pleural cavity, CNS, eyes – 0.9%
Peritoneal cavity, CNS, eyes – 0.9%	

(Pedersen, N.C. (2023) 2023 - neurological ocular FIP, Sock it to FIP)

Figure 2. Variability in clinical signs of non-effusive (dry) FIP

Signs referable to – % affected.

Peritoneal cavity – 30%	Peritoneal & pleural cavities – 4%
CNS – 22%	Peritoneal & pleural cavities, CNS – 3%
Eyes – 14%	Peritoneal cavity, eyes – 7%
CNS & eyes – 8%	Peritoneal & pleural cavities, eyes – 2%
Peritoneal cavity, CNS, eyes – 2%	Pleural cavity – 1%

(Pedersen, N.C. (2023) 2023 - neurological ocular FIP, Sock it to FIP)

Neurological FIP

According to studies by *Bradshaw J.M. et al,* FIP affects over 50% of cats with central nervous system (CNS) inflammation, and approximately one-sixth of all cats displaying CNS symptoms, irrespective of the underlying cause, are found to have FIP (Pedersen, N.C., 2008).

Neurological FIP can manifest in two distinct forms: primary and secondary. In primary neurological FIP, affected cats typically seek medical attention due to abnormal neurological symptoms. However, they often exhibit general signs of poor health such as lethargy, loss of weight, loss of condition and anorexia. Fever may or may not be evident. In the case of primary neurological FIP, approximately 50% of affected cats also present with discernible lesions beyond the central nervous system, and their haematological profiles tend to demonstrate a greater resemblance to systemic FIP. However, if these lesions do not venture outside of the CNS, we can see nearly normal values in CBC and serum chemistry tests.

Initial indicators of neurological FIP encompass manifestations such as floor or wall licking, tremors, seizures, anisocoria, and behavioural or cognitive aberrations such as confusion and aggression. With the advancement of these neurological manifestations, the suspicion of neurological FIP becomes more pronounced. Usually, the first discernible indication is a gradual decline in coordination and balance, frequently coupled with an aversion to jumping on or off elevated surfaces. At the outset, the primary impact is on hind leg coordination, which swiftly progresses to more widespread effects. Scientific literature has reported a range of symptoms including grand mal seizures, ataxia, abnormal posture, hyperesthesia, tetraparesis, central vestibular signs, cranial nerve deficits, central vestibular signs, cranial nerve deficits, abnormal mental status and abnormal behaviour (Diaz, J.V. and Poma, R. 2009).

On the contrary, in cases of secondary neurological FIP, cats initially display the characteristic systemic symptoms of the disease, with central nervous system (CNS) involvement manifesting at a later juncture. Neurological complications often arise during antiviral drug treatment for various FIP forms, potentially leading to relapses in cats receiving therapy for common systemic FIP. If relapse does occur it is most commonly seen 1-4 weeks after what seemed to be an effective therapy at the outset (Pedersen, N.C., 2021).

According to Dr. Niels C. Pedersen, spinal cord engagement often goes unnoticed in instances of neurological FIP, despite the fact that more than half of cats exhibiting inflammatory spinal cord disease are found to have FIP. (Pedersen, N.C., 2021). Such involvement can result in varying degrees of faecal and/or urinary incontinence and may present as paralysis of the tail or hindlegs. In contrast to brain-related issues, spinal cord involvement is more inclined to lead to enduring neurological impairments. Other clinicals signs of neurological FIPV that are worth mentioning include intention tremors, visual defects, complications with menace reflex, palsy of the cranial nerves, ependyma or ependymitis with hydrocephalus, dementia, encephalitis and myelitis.

Ocular FIP

As previously stated, ocular symptoms associated with FIPV are considerably more prevalent in the non-effusive variant of the disease. Interestingly, in some cases, ocular damage may be the initial clinical manifestation. This phenomenon is documented in approximately one-third of felines affected by non-exudative FIPV, with extraocular

symptoms observed in approximately two-thirds of cases (Figure 2). In contrast, it is relatively uncommon to have ocular involvement in cases of exudative FIPV (figure 1). Ocular involvement in FIPV can occur alone, with CNS or with lesions in the peritoneal cavity. As seen in figure 2, less than one-third of patients presenting with FIPV will also have neurological disease presentation. The primary ocular manifestations in dry FIP are unilateral or bilateral uveitis and chorioretinitis. FIP stands as a primary contributor to uveitis and chorioretinitis in cats, marked by the inflammation of the iris and ciliary body. Less frequent causes of uveitis include trauma, Feline Leukaemia Virus (FeLV) related lymphosarcoma, toxoplasmosis, and lens-associated uveitis (Pedersen, N.C., 2008). In a subset of felines with ocular FIPV, retinitis serves as a concurrent characteristic, presenting as localized tapetal hyporeflectivity linked to regional inflammation and minor haemorrhaging of retinal blood vessels. (Pedersen, N.C., 2021)

An early sign of ocular FIP is a change in the colour of the iris. Characteristic indicators include the deposition of keratin precipitates on the posterior cornea, arising due to the accumulation of fibrin, as well as macrophages and various other cells associated with inflammation. In some cases, focal lesions similar to parenchymatous organ granulomas may affect the shape of the pupil and iris. In cases where the outcome is enucleation, the leading lesions are usually glaucoma or panophtalmitis. These generally present unilaterally.

Other clinical manifestations of FIP with ocular involvement include aqueous flare, ocular discomfort, oedema of the cornea, hypopyon, hyphema, miosis, ocular hypotony, iridal hyperemia, neovascularisation, discharge, blindness, choroid lesions or plexitis with alterations in the segments, which encompass conditions such as chorioretinitis, perivascular cuffing, optic neuritis, and retinal detachment, all of which should be examined. Aqueous flare, signalling heightened protein levels within the anterior chamber, serves as a characteristic feature of anterior uveitis.

The neurological and/or ocular manifestations of FIP may exhibit clinical similarities to feline systemic toxoplasmosis, thereby prompting comprehensive evaluations for toxoplasmosis and administration of therapeutic agents such as Clindamycin or other antibiotics. Nevertheless, it is imperative to acknowledge that systemic toxoplasmosis is an infrequent ailment among feline populations, particularly when juxtaposed with the prevalence of FIP.

Understanding the blood- brain and blood-ocular barrier

The body's protective system known as the blood-brain barrier (BBB) acts to separate the brain and central nervous system (CNS) from the bloodstream. The BBB is primarily constituted by specialized cells and tight junctions between these cells. These structures play a pivotal role in meticulously controlling the transit of substances from the bloodstream into the brain and spinal cord. The preeminent function of the BBB lies in safeguarding the vulnerable neural tissue of the central nervous system (CNS) against detrimental substances, pathogens, and perturbations in the body's internal environment.

The presence of the BBB has significant implications for the treatment of neurological and ocular feline infectious peritonitis (FIP) because it can limit the penetration of therapeutic drugs into the brain and ocular tissues. FIP, particularly in its neurological and ocular forms, can lead to inflammation and damage within the brain and eyes, which necessitates the effective delivery of medication to these affected areas. In neurological FIP, the BBB can impede the entry of antiviral drugs into the brain, making it challenging to achieve therapeutic levels within the CNS. This reduced drug penetration can limit the effectiveness of treatment and may contribute to the difficulty of treating neurological FIP. Similarly, in ocular FIP, the presence of the BBB at the interface between the bloodstream and the eye can restrict the entry of drugs into the ocular tissues. This limitation can hinder the treatment of ocular manifestations of FIP, where the virus may be present in the eye. Overall, the blood-brain barrier presents a significant challenge in the treatment of neurological and ocular FIP because it restricts the delivery of drugs to the affected areas. Researchers and veterinarians may need to explore strategies to enhance drug penetration across the BBB to improve the treatment outcomes for these specific forms of FIP.

The compartmentalization of the disease between the central nervous system (CNS) and other anatomical regions offers a plausible explanation for the reduced likelihood of detecting aberrations in blood tests among cats afflicted with primary neurological disease or experiencing relapses during or following treatment for non-neurological Feline Infectious Peritonitis (FIP) Localized inflammation within protected regions such as the CNS is less likely to trigger a systemic inflammatory response. This, in turn, reduces the likelihood of substantial changes in blood parameters, including increased total protein and globulin levels, decreased albumin levels, and alterations in the albumin to globulin (A: G) ratio (Pedersen, N.C., 2023).

Diagnosis of Neurological and Ocular FIP

FIP diagnosis is known to be challenging especially in the dry form, where ocular and neurological involvement is more prevalent, as blood tests can show up as being unremarkable and there is no effusion in the abdomen or chest to sample. FIP is commonly misdiagnosed due to its non- specific clinical manifestations such as weight loss, anorexia, fever and effusion. This can also be said for its clinicopathological findings such as lymphopenia (55-77% of cases) (Barker et Tasker, 2022), neutrophilia (39-55% of cases) (Barker et Tasker, 2022), normocytic normochromic anaemia (37-54% of cases), hyperproteinaemia and hypergammaglobulinemia, elevated liver enzymes (ALT, ALP) and elevated bilirubin (Herrewegh, A.A.P.M. et al. 1995). The albumin-to-globulin (A:G) ratio on serum biochemistry is an important marker. A low A:G ratio (< 0.4) strongly suggests the likelihood of FIP. Conversely, a high A:G ratio (> 0.8) significantly diminishes the probability of FIP (Barker et Tasker, 2022) There are also no definitive tests for the diagnosis of FIP. The diagnosis gains increased certainty when we integrate the laboratory findings with other factors such as medical history and predispositions, physical examination, complete blood count (CBC) in conjunction with the alterations observed in blood tests.

Due to the grave nature of FIP, it is crucial that pet owners and veterinarians are as certain as can be in their diagnosis. Typically, in the case of neurological and ocular FIP, this diagnosis relies on recognising characteristic elevated protein levels, the presence of neutrophils, macrophages, and lymphocytes are among the alterations observed in the CSF and aqueous humor

Notably, affected cats frequently exhibit an elevated total protein concentration (average 9.4 g/L; median 3.6 g/L; ranging from 0.85 to 28.8 g/L), accompanied by an increased total nucleated cell count (average 196/μL; median 171/μL; ranging from 15 to 479/μL) (Pedersen, N.C.,2023). Neutrophils typically dominate the inflammatory cell population in most cases, while a combination of lymphocytes and neutrophils may be observed in a smaller proportion.

MRI proves valuable in diagnosing neurological FIP, particularly when combined with amnesis, clinical signs and CSF analysis. In a study conducted by Crawford, A.H. et al. in 2017, twenty-four cats neurological FIP confirmed with histopathology underwent MRI to delineate common characteristics. The study revealed that the most frequently observed clinical abnormalities were T3-L3 myelopathy and central vestibular syndrome.

Consistently, MRI scans revealed anomalies such as contrast enhancement in the meninges and ependyma, ventriculomegaly, syringomyelia, and herniation at the foramen magnum. Crawford et al. also analysed eleven CSF samples, all of which exhibited elevated total protein levels and total nucleated cell counts. Histopathological examinations revealed the presence of perivascular pyogranulomatous infiltrates, lymphoplasmacytic infiltrates, or both, particularly affecting the leptomeninges, choroid plexuses, and periventricular parenchyma. (Crawford, A.H. et al., 2017)

In terms of laboratory testing, a detectable IgG anti-coronavirus antibody titre in the CSF is a useful antemortem indicator of neurological FIP. Studies have found that a CSF titre of 1:640 or higher is indicative of FIP (Soma, T., 2017). Cats with these high titres were also found to be consistently positive by real-time polymerase chain reaction (RT-PCR) (Pedersen, N.C.,2023). Another important diagnostic aid particularly for neurological and ocular FIP cases when using CSF and aqueous humor samples is the detection of FCoV 7B. In a study of 95 serum samples, it was found that healthy cats with negative results in the immunofluorescence assay (IFA) for antibodies against the 7b protein were also negative for these antibodies. Additionally, certain healthy cats, despite having detectable Feline Coronavirus (FCoV)-specific antibodies through IFA, did not exhibit antibodies against the 7b protein. Cats diagnosed with Feline Infectious Peritonitis (FIP) were found to possess antibodies against the 7b protein, even in cases where conventional IFA yielded negative results. However, it's worth noting that some healthy cats and cats with conditions other than FIP, who tested positive for FCoV via IFA, also tested positive for the 7b protein antibodies. (Kennedy, M.A. et al. 2008)

Overview of the nucleoside analogue antiviral drug, GS-441524 (GS)

The compound GS-441524, known in scientific terms as (2R,3R,4S,5R)-2-(4-Aminopyrrolo[2,1-f][1,2,4]triazin-7-yl)-3,4-dihydroxy-5-(hydroxymethyl)tetrahydrofuran-2-carbonitrile, has been referred to by several alternative names throughout its history Within this report, the term 'GS-441524-like' is used to succinctly describe numerous unlicensed drug formulations that assert the presence of this compound, despite their origin not being associated with Gilead Sciences. GS-441524, a nucleoside analogue antiviral medication, was originally manufactured by Gilead Sciences. It functions as the primary plasma metabolite of the antiviral prodrug remdesivir and demonstrates an estimated half-life of roughly 24 hours in humans. Studies have explored the potential effectiveness of GS-

441524 and Remdesivir against a variety of RNA viruses, including coronaviruses such as SARS-CoV and MERS-CoV, as well as the Ebola virus. In certain countries, including the United States, Remdesivir obtained emergency use authorization for managing COVID-19. Both remdesivir and GS-441524 have demonstrated in vitro effectiveness against feline coronavirus strains responsible FIPV. While remdesivir has not been formally tested in cats (although some veterinarians now offer it) and despite not receiving official FDA approval for veterinary use due to Gilead's choice not to license it, GS-441524 has emerged as a widely utilized and effective treatment for FIP. When tested against SARS-CoV-2 in cell culture, GS-441524 demonstrates potency that is comparable to or even greater than that of remdesivir. Some researchers contend that GS-441524 could offer superior efficacy in treating COVID-19 compared to remdesivir. (Pruijssers, A.J., et al. 2020)

The nucleoside GS-441524 undergoes a phosphorylation process facilitated by nucleoside kinases. Following this, it undergoes an additional phosphorylation process facilitated by nucleoside-diphosphate kinase (NDK) to achieve its nucleotide triphosphate active form. It disrupts the ongoing viral RNA synthesis process by competing with native nucleoside triphosphates, leading to the premature cessation of RNA polymerase-mediated transcription (Jones, S., et al, 2021)

Currently, no approved therapeutic intervention has been identified to combat the lethal ailment, FIP. Dr. Niels C. Pedersen has reported various studies where the efficacy of drugs such as Tylosin, prednisolone, phenylalanine mustard, cyclophosphamide, feline interferon omega, immunostimulants, vitamins, nutraceuticals and pentoxifylline has been tested, but have been observed to merely postpone the inevitable progression of the disease and no veterinary drug regimen has been proven effective with time. He also notes that effective treatments have been as hard to find as effective vaccines. (Pedersen, N.C., 2008). However, Pedersen undertook a research investigation aimed at assessing the safety and effectiveness of the nucleoside analogue GS-441524 for cats afflicted by diverse manifestations of naturally occurring Feline Infectious Peritonitis (FIP). This study involved a cohort of 26 cats with wet or effusive FIP and 5 cats with the dry or non-effusive form of the disease. The findings established that the treatment with GS-441524 yielded results surpassing initial expectations, suggesting that FIP, regardless of factors like signalment or disease presentation, can be managed with the use of nucleoside analogues. (Pedersen, N.C., 2019)

In terms of utilization and research, GS-441524 has made its way to the black market, where pet owners are using it in their efforts to treat FIP, given the typically fatal nature of the disease and the absence of approved treatments. This usage occurs despite Gilead Sciences' refusal to authorize the drug for veterinary purposes, despite conclusive results.

The pricing for injectable medications varies, with each vial ranging in cost from $65 to $120, working out at a mean of 4920 USD or 4685 EUR for the 84-day treatment, contingent upon the specific brand and the potency of the medication. The daily dosage required is dependant not only upon the cat's body weight but also the particular manifestation of feline infectious peritonitis (FIP) that afflicts the cat. To obtain an approximate cost estimation for a 12-week course of treatment, an online calculator is available for cat owners at the following link: https://fiptreatment.com/dose-calculator/.

Currently, GS-441524 is accessible in three different concentrations: 15mg/ml, 17mg/ml, and 20mg/ml. The recommended dosage depends on the specific clinical presentation of feline infectious peritonitis (FIP). For cases of wet or dry FIP without ocular or neurological involvement, the suggested dosage for subcutaneous injection is between 5mg/kg and 6mg/kg. In instances of ocular FIP, whether occurring alongside wet or dry FIP, a minimum dosage of 8mg/kg is advised. Neurological FIP cases are typically treated with a minimum dosage of 10mg/kg. In cats, the blood-brain barrier typically hinders the penetration of around 80% of most medications, while the blood-eye barrier restricts approximately 70% of these substances. As a result, if a specific drug dosage, when a compound, such as GS-441524, reaches an effective plasma concentration of 10 µM, its levels in the cerebrospinal fluid of the brain will decrease to 2 µM, and within the aqueous humor of the eye, it will drop to 3 µM. In the event of relapses, it is recommended to administer a dosage that is 5mg/kg higher than the initial prescribed amount. Occasionally, for difficult cases a dosage above 15mg/kg is used. (FIP warriors and Pedersen, N.C. (2023) In cases where both injectable and oral tablet forms of the GS is being used the protocol advises that, following an initial 2-week course of daily injections with the prescribed dosages for effusive and ocular forms, or a 2–4-week regimen for the neuropathic form, the option of transitioning to oral GS-441524 tablets becomes available if ascites is not present. This strategy is aimed at cost reduction and the minimization of treatment-related side effects (Garrido-Andersson, L., 2022).

When mentioning such side effects, it is important to note that recent studies have identified a novel type of urolith in cats treated with GS-like drugs. Unlike typical uroliths rich in phosphorus, magnesium, and calcium, these stones are high in oxygen, nitrogen, and carbon. GS drugs are primarily excreted in urine, increasing the risk of stone formation. Veterinarians should monitor cats for urinary issues when administering these drugs. Adjusting the dosage to prevent stone formation can be complex, especially for cats with neurological and ocular FIP, as reducing the dose may lead to complications like incontinence. (Minnesota Urolith Centre, 2023)

GS-441524 is available in both injectable and oral forms. The oral GS-441524 demonstrates an absorption efficiency of less than 50% in comparison to the injectable form, necessitating a doubling of the oral dose. Manufacturers of oral GS-441524 seldom reveal the actual concentration in their tablets or capsules. Instead, they label them as an equivalent dose to the injectable form. Additionally, the oral GS-441524 absorption efficiency has an upper limit, making it challenging to achieve the elevated blood levels necessary for effective drug distribution into the brain and eyes. Therefore, in cases where unsatisfactory results are observed in cats with ocular and neurological conditions, even with high equivalent oral doses of GS-441524, transitioning to the injectable form is recommended (Pedersen, N.C., 2023).

A favourable response is anticipated with any dosage escalation, and a lack of improvement suggests that the dosage remains insufficient, potential drug resistance is emerging, the GS brand may not meet expectations, the cat might not have FIP, or other underlying conditions could be complicating the treatment.

Difficulty still lies in knowing when to stop treatment. Although the recommended time of treatment is 12 weeks or 84-days, many cats can show complete symptomatic improvement and clear laboratory findings before the full duration of treatment. It is speculated but not confirmed that the cats own immunity to FIPV may build at around week 8-10 of treatment. (Pedersen, N.C., 2023)

Retrospective and Prospective Study

Aims

The primary objective of this thesis is to advance our understanding of the less common manifestations of Feline Infectious Peritonitis (FIP), specifically the neurological and ocular forms, and their treatment utilizing the antiviral nucleoside analogue GS-441524.

Evidently, there has been a notable surge in the number of pet owners turning to this unlicensed medication in a desperate bid to save their beloved feline companions. However, it is concerning that these private trials and treatments are not being formally documented within the scientific community. Furthermore, the majority of recorded treatments predominantly focus on the wet form of FIP, neglecting cases with neurological or ocular involvement.

To address this knowledge gap and provide more comprehensive insights into the outcomes of such treatments, I have developed an online questionnaire. This questionnaire is designed to be entirely anonymous, inviting input from pet owners, veterinarians, or anyone involved in the treatment of cats afflicted with neurological or ocular FIP and treated with GS-441524- like drugs. The survey consists of 31 questions and is intended for individuals who have either completed treatment or are currently undergoing treatment for their cats with neurological or ocular FIP.

Research Protocol- Methods and Materials

Survey structure

To broaden the reach to a wider audience, three versions of the survey were developed in English, Hungarian, and French. The survey was crafted using the crowdsignal.com platform and incorporates a combination of 'yes' or 'no' questions, multiple-choice questions, and open-ended responses. The questions were structured in the following manner:

1. What is the cat's name?
2. What is the sex of the cat?
3. What is the breed of the cat?
4. Is the cat spayed/ castrated?
5. What country does the cat originally come from?
6. What country does the cat currently reside in?
7. How old was the cat when diagnosed?
8. Did the cat have contact with other cats prior to diagnosis?
9. How many cats were in the household?
10. Has the cat ever had a litter, if so, how many litters?
11. Did you know the cat had Feline Coronavirus prior to its mutation to FIP?
12. What type of FIP does the cat have? Please specify in the comments if it is dry or wet form with neurological or ocular signs.
13. Were there any predisposing conditions? E.g., Stressful situations, vaccinations, spaying or castrating, overcrowding, immunosuppression, poor nutrition etc. If yes, please specify.
14. What symptoms were displayed by the cat?
15. Did the cat have any other illnesses prior to the FIP diagnosis? If yes, please specify.
16. How was the cat diagnosed?
17. Did the cat receive other medications for FIP or symptoms prior to or during the treatment with GS-441524? If yes, please specify.
18. How did you find out about GS-441524?
19. Did you find it difficult to source GS-441524?
20. How long did it take to begin treatment with GS-441524 from the time of diagnosis?
21. What form of GS-441524 did you use?
22. What was the starting dosage of the cat? (mg/kg) What was the ending dosage of the cat (mg/kg)? If the ending dosage if different, please explain at what specific point(s) during treatment it increased and by how much. What prompted the increase(s)?
23. What was the duration of treatment?
24. What was the protocol for administration? (times, injection sites, before or after feeding etc.)
25. How accurate/ consistent were you with administration protocol?
26. Did the cat receive health checks during treatment?
27. Did you notice any adverse effects, side effects or reactions during or after treatment?
28. How long did it take for you to notice a positive impact of GS-441524 on the health of the cat after starting treatment?
29. What changes did you notice in the health of the cat?
30. If your cat has finished treatment, has there been any signs of relapse?
31. Did your cat survive this disease following treatment?

Dissemination of survey

The survey was open to responses from the 10th of September to the 5th of October, receiving 226 total responses. However, only 190 of these responses fulfilled the inclusion criteria, meaning they pertained to cats afflicted with neurological or ocular FIP, treated with GS-441524, and the surveys were completed in their entirety. The survey was shared via email to numerous veterinary clinics, medical journals and FIP specialists, however, the largest response was received through Facebook FIP support groups such as FIP Warriors ® which has over 52.6k members, FIP Global CATS (Community, Advocacy, Treatment, Support) and other similar groups. The members of these online support groups include owners of cats who have undergone or are undergoing treatment, veterinarians, FIP specialists, administrators and more. The group administrators exercised a stringent and cautious approach when granting me access to their communities, prioritizing the safeguarding of member data. Simultaneously, they displayed exceptional dedication and cooperation in assisting me with the dissemination of my survey, aiming to maximize its outreach and collect precise, valuable insights.

Thanks to the support of these groups, the survey reached respondents in a total of 18 countries.

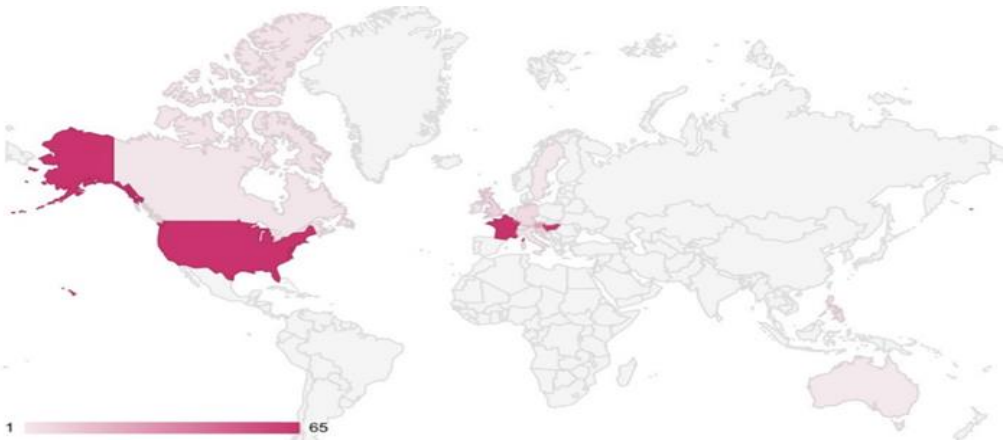


Figure 3. Map of participants (Crowdsignal, 2023)

France had the highest number of responses, with 65 participants, accounting for approximately 28.76% of the total. The United States closely followed with 63 responses, constituting around 27.88% of the total. Hungary contributed 28 responses (12.39%), while Austria provided 27 responses (11.95%). The United Kingdom yielded 9 responses (3.98%), Belgium had 7 responses (3.10%), and Germany received 6 responses (2.65%). Additionally, Slovenia and the Philippines

each contributed 5 and 3 responses, respectively, making up around 2.21% and 1.33% of the total. Canada and Italy had 3 and 2 responses, respectively, comprising 1.33% and 0.88%. Australia, Ireland, Sweden, Luxembourg, and Slovakia each provided one response, contributing 0.44% of the total. There was also one response from a participant located in 'Europe,' which accounted for 0.44% of the survey's total responses.

Results

I. Sex

Among the 190 cats analysed, 130 cats (68.4%) of cats were male and 60 cats (31.6%) were female. This can be visualised in figure 4.

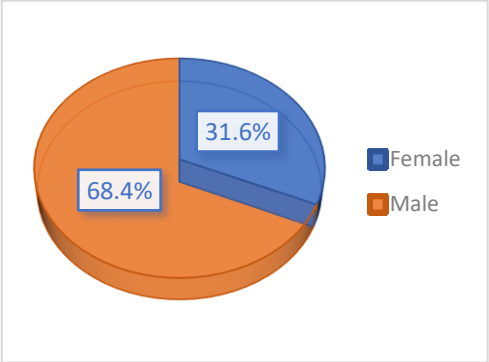


Figure 4. Sex of cat

II. Breed

In this scientific analysis, the majority of feline subjects (58.9%) were representative of domestic household cats, encompassing both short and long-haired varieties. Notably, Maine Coon cats accounted for 11% of the sampled population, while British Shorthairs constituted 5.79% of the recorded cases.

Birmans were observed in 3.68% of instances, closely followed by Ragdolls at 3.16%. Siberian cats and Devon Rexes were each encountered in 2.63% and 2.11% of cases, respectively. Russian Blues, American Bobtails, and Bengals each made up 1.05% of the cases. Several other breeds, such as Arabian Mau, Balinese, Bombay, Burmese, Munchkin, Norwegian Forest Cat, Oriental, Persian, Puspin, Snowshoe, Sphynx Elf, and Tonkinese, were each represented in just one individual case, constituting 0.53% of the overall sample each. This can be seen in figure 5.

Breed	Count	Percentage
Domestic short hair	106	58.9%
Maine Coon	21	11.05%
British short hair	11	5.79%
Birman	7	3.68%
Ragdoll	6	3.16%
Siberian	5	2.63%
Devon Rex	4	2.11%
Russian Blue	2	1.05%
American Bobtail	2	1.05%
Bengal	2	1.05%
Balinese	1	0.53%
Arabian Mau	1	0.53%
Bombay	1	0.53%
Burmese	1	0.53%
Munchkin	1	0.53%
Norwegian forest cat	1	0.53%
Oriental	1	0.53%
Persian	1	0.53%
Puspin	1	0.53%
Snowshoe	1	0.53%
Sphynx elf	1	0.53%
Tonkinese	1	0.53%

Figure 5. Breeds

III. Neuter Status

Amongst the 190 cases analysed, 161 (84.74%) of these cats were either spayed or castrated. One case involved chemical castration (0.53%). In 28 (14.74%) cases reported their cat was entire. These numbers can be visualised in figure 6.

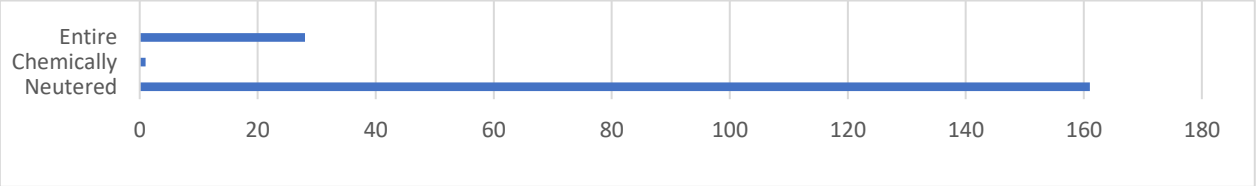


Figure 6. Neuter status.

IV. Type of FIP

As illustrated in Figure 7, among the 190 neurological or ocular FIP cases under examination, 104 (54.74%) exhibited neurological involvement. In these neurological cats, 67 (35.36%) of the cases were classified as non-effusive/dry FIP and 37 (19.47%) were effusive. Furthermore, 49 (25.79%) of cases had ocular involvement. Among these ocular FIP cases, 38 (20.00%) of these cases presented with non-effusive/ dry FIP and 11 (5.79%) of cases were effusive/ wet.

Notably, 37 (19.47%) of cases had both neurological and ocular involvement with 30 (15.79%) being non-effusive/ dry FIP and 7 (3.68%) of cases being effusive/wet FIP.

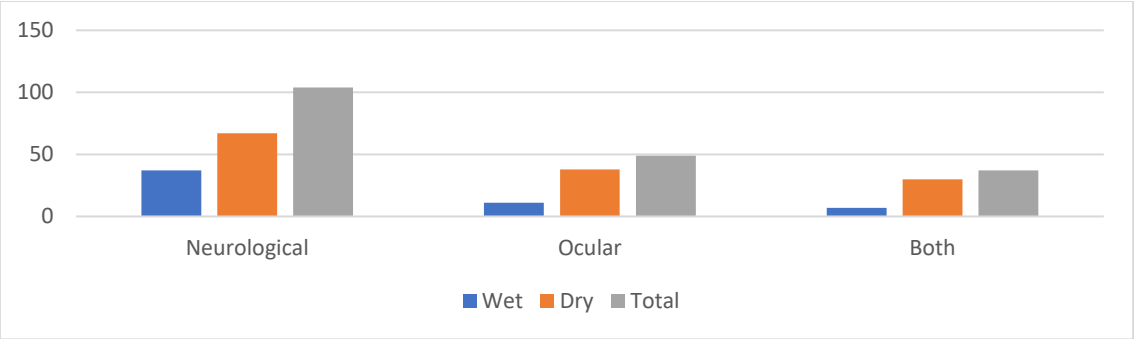


Figure 7. Types of FIP

V. Age upon Diagnosis

The survey showed that 42% of cats were diagnosed under the age of 6 months with a notable 15% of this being at the 6-month-old mark. 30% of cats were diagnosed between

6months – 12 months old. Furthermore, 18% of cases were between 12 months and 24 months of age when diagnosed. 8% of cases were between the ages of 24 months- 36 months (3 years). The remaining 2% were aged 3-9 years with one outlier being 15 years old.

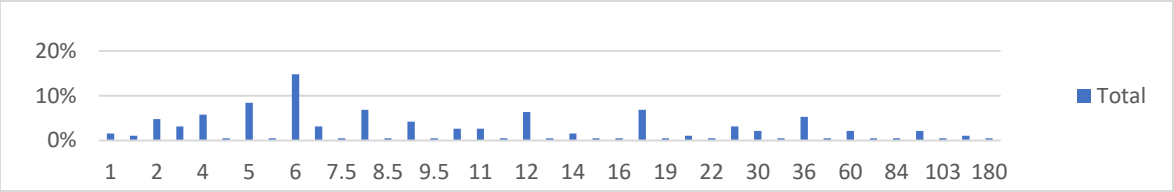


Figure 8. Age upon diagnosis (months)

VI. Contact with other cats prior to diagnosis

According to the survey findings, 166 (87.37%) of the cats had been in contact with other cats before being diagnosed, while the remaining 24 (12.63%) had no prior contact with other felines.

VII. Number of cats in household

The distribution of cats within households, as observed in the dataset, reveals a diverse range of compositions. Approximately 21.05% of households had only one cat, while the majority, comprising 36.84%, had two cats. Households with three and four cats each accounted for 11.05% of the cases. Smaller percentages were attributed to households with five (2.11%), six (3.16%), seven (2.11%), and eight (1.05%) cats. An even smaller fraction of households, at 0.53%, had nine or thirteen cats. Approximately 2.63% of households had ten cats, with an additional 2.11% having eleven cats. Further, 0.53% of households housed fourteen cats. A notable 2.11% of households had twenty cats, while 0.53% had twenty-three cats. Larger households with thirty cats represented 1.58% of the cases, and those with fifty cats constituted 1.05% of the total dataset. This can be seen in figure 9 below.

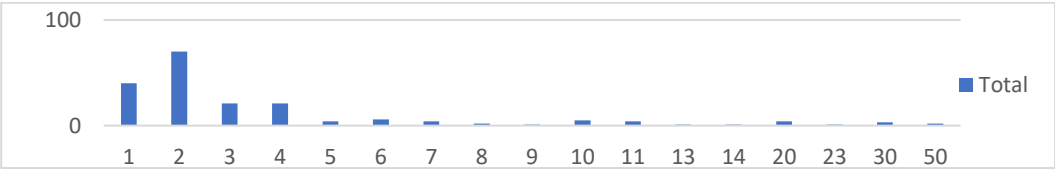
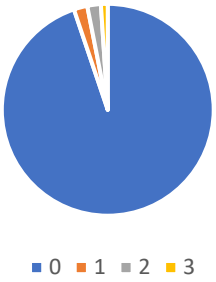


Figure 9. Cats per household

Figure 10. Number of litters per cat (females)



VIII. Number of litters

Excluding the 130 male cats, out of the 60 female cats with neurological or ocular FIP 55 (91.6%) of the females had no litters, 2 (3.3%) had 1 litter, 2 (3.3%) had 2 litters and 1 (1.6%) had 3 litters.

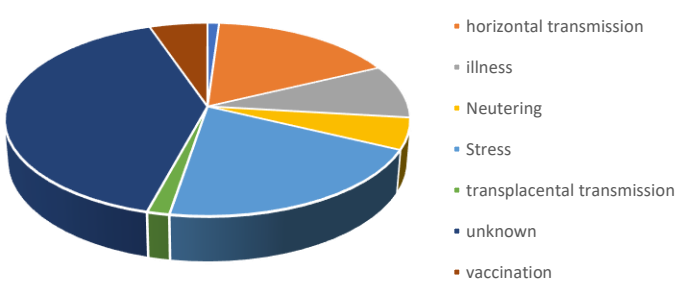
IX. Awareness of being infected with Feline Coronavirus prior to its mutation to FIP

When participants were asked if they were aware of the FCoV status of the cat prior to its mutation to FIP, 178 (93.6%) of owners said they were unaware. The remaining 12 (6.3%) said yes, they were aware.

X. Predisposing conditions

When asked about perceptions regarding the possible factors contributing to the feline coronavirus (FCoV) mutation to FIP, the respondents' answers were as follows. "Unknown" was the most frequently cited factor, with 77 respondents, comprising 40.5% of the responses. Stress was the second most commonly mentioned factor, pointed out by a substantial 39 respondents, accounting for 20.5% of the total. Horizontal transmission came in third place, cited by 32 individuals, making up 16.8% of the responses. Illness was identified as a potential cause by 17 respondents, representing 8.9% of the surveyed population. Neutering was attributed to FIP by 10 individuals, making up 5.3% of the answers. Vaccination was mentioned by 10 respondents as well, accounting for another 5.3% of the surveyed population. Genetic factors were identified by only 2 respondents, constituting a mere 1.1% of the total surveyed. Transplacental transmission was noted by 3 individuals, amounting to 1.6% of the responses. This is shown on figure 12.

Figure 11. Predisposing factors

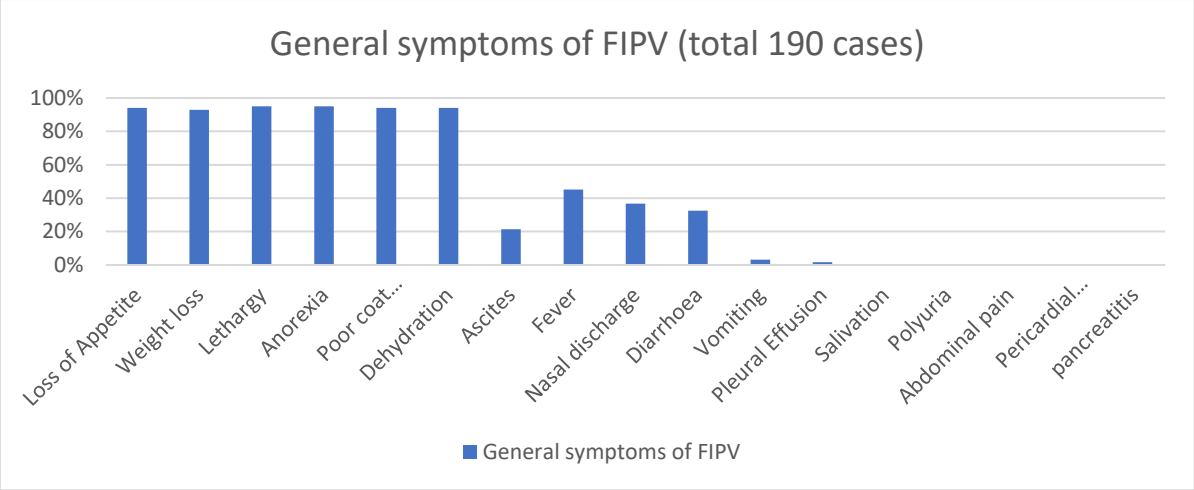


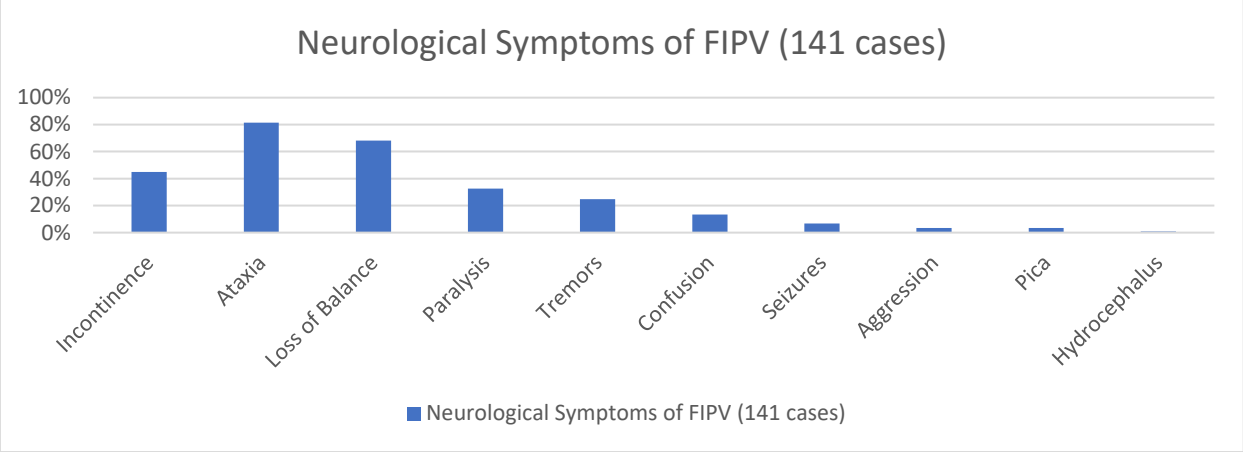
XI. Symptoms

When it came to the symptoms of the cats in the survey, several patterns were observed in the dataset. The symptoms will be broken down into three charts within figure 12. Representing general, neurological and ocular symptoms that occurred in these cases. Predominantly, loss of appetite was the most frequently reported symptom, occurring in 179 out of 190 cases, representing a substantial 94% of the cases. Similarly, weight loss was highly prevalent, affecting 176 cases, or 93% of the total instances. Lethargy was a pervasive symptom, reported in 181 cases, which accounted for 95% of the occurrences. Poor coat condition was also notably common, impacting 179 cases, or 94%. Anorexia, another significant symptom, was observed in 181 cases, also representing 95% of the instances. Dehydration was seen in 179 cases, equivalent to 94% of the dataset. Fever, a notable symptom, was recorded in 86 instances, making up 45.2% of the cases. Nasal discharge was reported in 70 cases, accounting for 36.8% of the occurrences. Diarrhea was reported in 62 cases, making up 32.6% of the dataset. Ascites was seen in 41 (21.5%) cases. Other less common symptoms such as vomiting (3.20%), pleural effusion (1.60%), salivation (0.50%), polyuria (0.50%), abdominal pain (0.50%), pericardial effusion (0.50%) and pancreatitis (0.50%) were also observed.

In the 141 neurological cases, symptoms included incontinence was seen in 64 cases (45%). Ataxia was observed in 115 cases, making up 81.5% of neurological cases. Loss of balance was reported in 96 cases, constituting 68.08% of the neurological cases. Paralysis affected 46 cases, contributing to 32.62% of the neurological dataset. Tremors were observed in 35 instances, comprising 24.82% of the neurological cases. Confusion was present in 19 cases, accounting for 13.47% of the occurrence. Seizures were reported in 6.83% of neurological cats. Less common symptoms included aggression (3.54%), pica (3.54%) and hydrocephalus (0.71%)

In the 86 FIP cases that had ocular involvement the following symptoms were seen. Ocular discharge was noted in 52 cases, or 60.4% of the ocular instances. 51 cases (57.3%) presented with uveitis. Corneal opacity was seen in 17 (19.76%) of ocular cases. Blindness was reported in 9 (10.46%) of the ocular cases. In 8 cases (9.30%) anisocoria was mentioned. Less common symptoms, such as ocular bleeding (8.13%), nictitating membrane prolapse (6.98%), miosis (1.16%), conjunctival hyperemia (4.65%) and blepharospasm (3.49%) were also mentioned in the FIPV cases with ocular involvement.





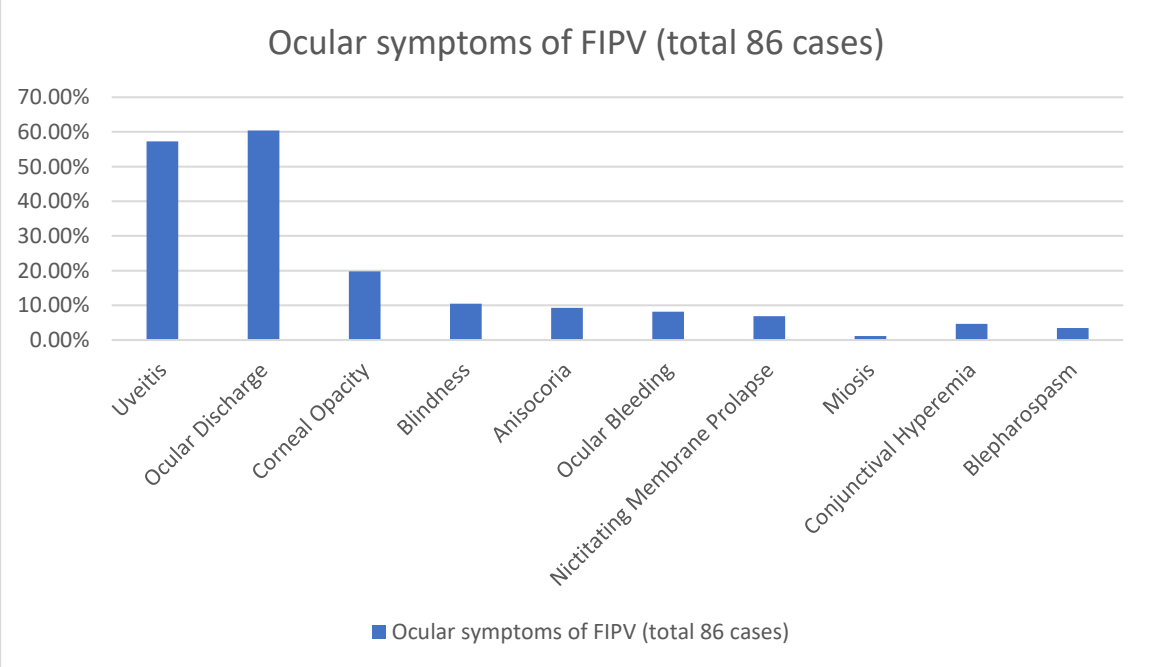


Figure 12. Symptoms in general, neurological and ocular FIPV cases.

XII. Other prior illnesses

The most prevalent category among the 190 surveyed cats was no prior illness, with 129 (67.9%) cats. Following that, the second most common condition was upper respiratory infection, which affected 12 (6.3%) cats. Other frequently reported conditions included FIV with 5 cases (2.6%), Gastroenteritis with 4 cases (2.1%), Coryza with 3 cases (1.6%), and Giardia with 3 cases (1.6%).

Less common health conditions observed among the surveyed cats included herpes and ringworm, each reported in 3 cases (1.6% each). FeLV was documented in 2 cases (1.1%), as was Periodontal disease with 2 cases (1.1%). Several conditions appeared in only one case each, making up the remaining 3.7% of the surveyed cats, including anaplasmosis and FELV, Cerebellar hypoplasia, Coccidiosis, Conjunctivitis, Ear mites, FORL (Feline Odontoclastic Resorptive Lesions), Lethargy, Leukosis, Mouth ulcer, Ocular illness, Otitis (Ear Infection), Paraplegia, Pneumonia, Rhinotracheitis, Spinal infection, Toxoplasmosis, Unknown flu-like symptoms, UTI (Urinary Tract Infection), and weak kitten. These conditions individually represented 1.1% of the total cases each.

XIII. Method of diagnosis

The most common diagnostic method mentioned in the 190 surveys about cats with FIP was Laboratory Examination, which was used in 54.74% of cases (104 times). This includes checking parameters such as WBC (white blood cell) counts, neutrophils, monocytes and lymphocytes, A:G ratio, creatinine, BUN (blood urea nitrogen) and ALT (alanine transaminase). Following closely was PCR (Polymerase Chain Reaction), employed in 44.21% of cases (84 times). Ultrasound was the third most frequently mentioned method, utilized in 17.89% of cases (34 times). Clinical Signs were a significant diagnostic factor in 24.21% of cases (46 times), while Blood Tests were used in 13.16% of cases (25 times). Radiography was conducted in 12.11% of cases (23 times). MRI (Magnetic Resonance Imaging) was employed in 11.05% of cases (21 times), and Biopsy was also used in 11.05% of cases (21 times). Antibody Testing played a role in 13.68% of cases (26 times). Some less common diagnostic methods included CSF Sampling and CT Scans, each utilized in 3.68% of cases (7 times). The Rivalta Test, Abdominocentesis, and Electrophoresis were employed in 1.58% of cases (3 times each). Ocular Examination and Self Diagnosis were the least common, each mentioned in 0.53% of cases (1 time each). Process of Elimination was utilized in 4.21% of cases (8 times).

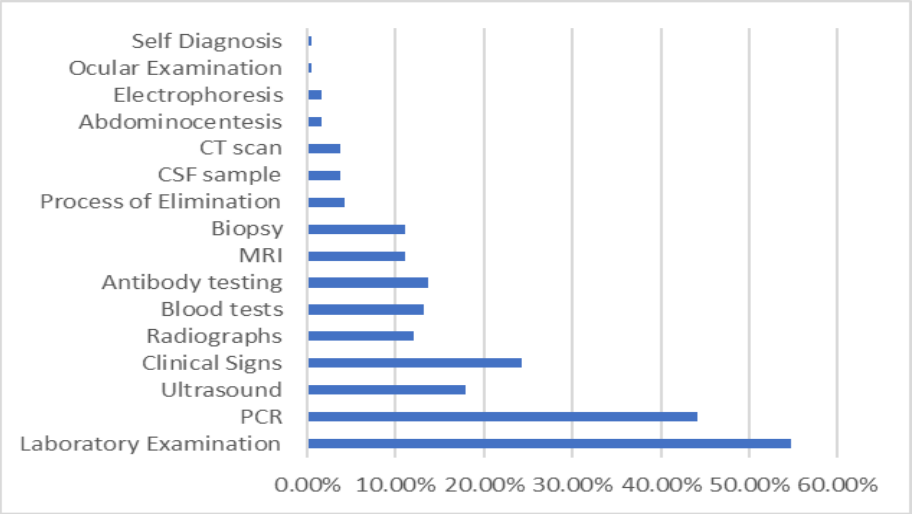


Figure 13. Method of diagnosis

XIV. Concomitant medications

Surprisingly, the majority of cats in the dataset, which is approximately 57.9%, received no specific treatment after their neurological or ocular FIP diagnosis concurrent with the GS therapy. This may reflect varying treatment strategies, the severity of the condition, or a watchful waiting approach.

According to the survey, antibiotics were administered to 53 cats (27.9%) of the total (190). These antibiotics included cefovecin, ampicillin, tobramycin, amoxicillin-clavulanic acid, clindamycin, chloramphenicol, neomycin, ofloxacin, cyclosporin, enrofloxacin, metronidazole, and azithromycin, indicating that a significant portion of the cats received antimicrobial treatment following their neurological or ocular FIP diagnosis. Approximately 42 (22.1%) of the cats received a hepatoprotectant. Anti-nausea medications, or antiemetics, were given to 13 cats (6.8%). Cerenia (maropitant citrate) was the specific antiemetic used in the treatment of these cats. Corticosteroids were employed in the treatment of 54 (28.4%)) of the cats, particularly prednisolone and methylprednisolone. Non-steroidal anti-inflammatory drugs (NSAIDs) were prescribed to 9 cats (4.7%). These medications included meloxicam and robenacoxib. Kidney supplements were given to only 1 cat, representing approximately 0.5% of the total, suggesting that this treatment was not commonly employed in the dataset. About 4.7% of cats received B12 supplementation, totalling 9 cats, as a part of their treatment plan. Omega-3 supplementation was administered to 3 (1.6%) cats. Probiotics were prescribed

to 8 cats (4.2%). Mirtazapine, an appetite stimulant, was used in the treatment of 11 cats (5.8%). Erythropoietin, aimed at stimulating red blood cell production, was given to 2 cats (1.1%). Antipyretic medication, designed to reduce fever, was administered to 2 cats (1.1%). Tropicamide, an eye medication, was used for 1 cat (0.5%). Famciclovir was given to 3 cats (1.6%). Pain relief medications were administered to 25 cats, making up around 13.2% of the dataset. These medications included gabapentin, robenacoxib, and buprenorphine. Only 1 cat, approximately 0.5%, received plasmalyte and dextrose. Similarly, GC376, iron, taurine, and zinc were each administered to 1 cat, accounting for about 0.5% each. Seizure medications, including levetiracetam, phenobarbital, and potassium bromide, were prescribed to 3 cats, making up about 1.6% of the dataset. Molnupiravir was given to 2 cats (1.1%). Hartmann's solution was used in the treatment of 3 cats (1.6%). Only 1 cat received retromad, an antiviral drug accounting for about 0.5% of the cases. Approximately 10 (5.3%) of the received eye drops as a part of their treatment although the precise drugs used were not specified. A diuretic, Furosemide, was used for 1 cat (0.5%). Immunostimulants, such as polyprenyl, were administered to 4 cats, representing about 2.1% of the dataset. Only 1 cat received remdesivir, an antiviral medication, accounting for about 0.5% of the total. The analysis reveals that while the majority of cats received no specific treatment after diagnosis, a variety of medications and treatments were employed in smaller proportions for different purposes.

XV. Discovering GS- like therapy and sourcing the drug

The process by which owners become aware of GS-like therapy as a treatment option is intriguing, given the constraints on veterinarians to dispense unlicensed drugs. Nevertheless, there are no legal prohibitions preventing them from endorsing or suggesting it. When survey participants were queried about how they came across information about GS therapy, the following was discovered. A significant portion of respondents, 56 individuals (29.47%), mentioned that they were introduced to it through social media platforms like Facebook and support groups. A further 21 participants (11.05%) reported stumbling upon information related to the drug while browsing online, such as in articles, forums, or blogs. Interestingly, 3 cat owners (1.58%) mentioned that their initial exposure to this treatment came through personal contacts. Additionally, 7 participants (3.68%) indicated that they learned about GS-like therapy via rescue organizations, charities, or animal shelters. It's worth noting that the most prevalent response was provided by 90 participants (50.53%), who learned about GS-like therapy directly from their own veterinarians. When participants were asked if they

found it difficult to source the drug the overwhelming answer with 167 (87.89%) responses was no. 23 participants (12.11%), responded yes, they did find it difficult to get the drug.

XVI. Timeframe between diagnosis and initiating therapy with GS

According to the survey, 58 (30.53%) of owners had the medication in their possession within only hours of the neurological or ocular FIP diagnosis. Additionally, 115 (60.53%) had the drug within a few days of the diagnosis. 11 (5.79%) of owners reported receiving the GS-like drug within weeks of the diagnosis while a patient 6 individuals (3.16%) reported a somewhat protracted waiting period, spanning several months, before obtaining the treatment.

XVII. Form of GS-like medication used

GS- like medication is available in injectable, tablet and oral solution forms. From the survey it was seen that 109 (57.67%) of owners used the injectable form which is administered subcutaneously. The tablet form was used alone in only 11 cases (5.82%) while the oral solution was used even less, showing up in only 6 cases (3.17%). 2 cases (1.05%) of cases commented that they tried the tablet form and it did not work so they then switched to the injectable. Both the injectable and oral forms were used at different stages of the treatment in 63 cases (33.33%).

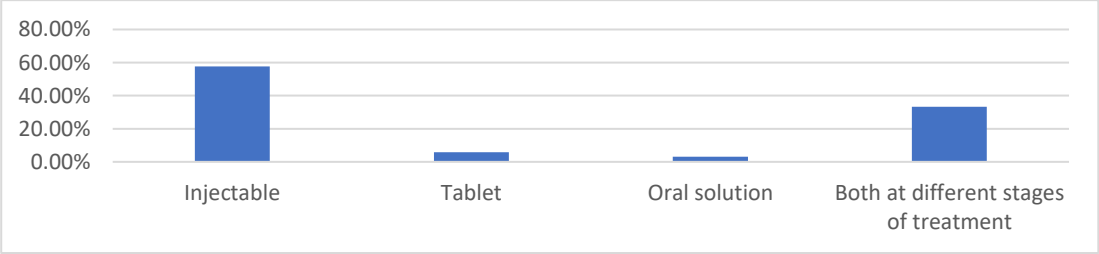


Figure 14. Form of GS

XVIII. Duration of treatment

As the recommended duration of treatment with GS-like therapy is 84 days, it is no surprise that the most common answer was this, with 96 (50.53%) of responses. During completion of the survey 28 (14.74%) were still undergoing treatment, although the majority of these were far into treatment, they are not included in figure 15 as it is unknown if their treatment time will be extended past the 84-day mark. 12(6.32%) of participants reported treatment lasting for 90 days. The remaining outliers can be seen in figure 15 where some treatments lasted from 91-160 days depending on the improvement of the individual patients and

potential relapses. This accounted for 30 (15.78%) of responses. On the other hand, in 10 responses (5.2%), treatment courses finished early. This have been due to death, finishing early once the symptoms subsided, which is not recommended, or perhaps treatment was still ongoing and the survey question was misinterpreted.

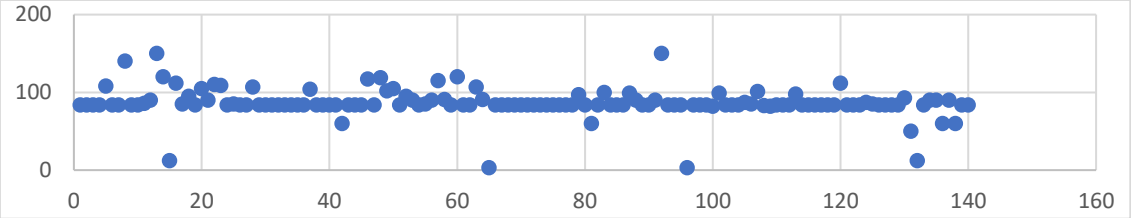


Figure 15. Duration of treatment (days)

XIX. Protocol for administration and owner accuracy

The administration of GS therapy adheres to a rigorous set of guidelines, emphasizing consistency and the well-being of the feline patients. It is highly recommended for cat owners to maintain a regular daily schedule for medication administration. Furthermore, for the subcutaneous injection form of the treatment, careful site rotation is advised to minimize potential irritation. A notable 142 (74.7%) of the owners, reported administering the medication after the cat's feeding. This routine practice aligns with the prescribed guidelines and ensures that the drug is given under optimal conditions. In 13 (6.84%) of the cases, owners commented that they required assistance from their veterinarians for the administration of the drug due to their inability to do it themselves. This underscores the importance of professional involvement in specific cases. Additionally, 6 responses (3.15%) of cases, reported administering the drug twice daily, showcasing variations in the administration regimen that might be tailored to individual cat's needs or conditions. This flexibility in dosing patterns ensures that treatment can be effectively customized to suit the requirements of each patient.

In terms of adhering to a strict regimen for administering the drug, the majority of owners demonstrated commendable compliance. Precisely 118 owners (62.11%) asserted that they followed the administration protocol ‘perfectly’. Furthermore, 69 participants (36.32%) reported being ‘good’ in adhering to the administration guidelines. In a small number of cases, only 2 (1.05%), the participants admitted to being ‘fair’ when it came to the guidelines. In just one instance (0.53%), the owner candidly acknowledged being ‘poor’ in maintain strict administration practices.

When it came to determining the dosage for each patient, many owners tended to confuse the terms "dosage" and "dose." However, correctly answered surveys revealed a dosage range of 10mg/kg to 54mg/kg, with a median starting dosage of 15mg/kg. Furthermore, it was observed that approximately 55% of cases, primarily those involving neurological FIP, required an increase in dosage during treatment due to either a lack of improvement or worsening clinical signs. In such cases, *Pedersen* recommends daily dosage increases of 2-5mg/kg for a minimum of 28 days.

XX. Medical monitoring throughout treatment

The survey conducted in this study provided a comprehensive perspective on the assessment veterinarians and owners alike were carrying out on these neurological and ocular FIP cases during the treatment. This was imperative to ensure the treatment was working and that the dosage and the duration of treatment did not need to be altered. Weight checks, conducted in all 190 cases (100%), served as a fundamental element of health monitoring. In all cases, as the cat gained weight, the dosage was increased. In 9 cases (4.74%), no additional diagnostic tests or procedures beyond weight checks were reported. This may suggest that some cases did not necessitate further diagnostic measures due to the nature of their conditions.

Biochemistry tests were routinely done in 178 cases (93.68%). Furthermore, Complete Blood Count (CBC) tests were carried out in 154 cases (80.53%). These blood tests were done every two weeks throughout treatment in the majority of cases. Ultrasound examinations were conducted in 28 cases (14.74%). From the French surveys, 19 cases (9.95%) reported that electrophoresis was carried out. Echocardiograms were carried out in 2 cases (1.05%). Abdominocentesis performed in 8 cases (4.21%). Fine-needle aspiration (FNA) of lymph nodes was conducted in 1 case (0.53%). A single urinalysis test was conducted (0.53%). In addition, a computed tomography (CT) scan was conducted in 1 case (0.53%), and a single Magnetic Resonance Imaging (MRI) test was performed (0.53%). Consultations with an ophthalmologist were sought in 4 cases (2.11%), to monitor progress in cases with ocular FIP.

XXI. Treatment related complications

Upon analysis of the data on the reported side effects of GS-like therapy in cats with neurological and ocular FIP the following was discovered. A significant portion of participants, 30 in total, did not report any side effects, accounting for 15.79% of the surveyed cases. This suggests a substantial number of cats experienced no adverse effects during the treatment.

Injection site reactions were the most commonly reported side effect, with 88 cases (46.32%) noting some form of reaction. This includes various complications such as **sores** at the injection site in 39 (20.53%) of cases. Figure 16. Shows images of such sores provided by FIP Warriors ®, 2023. **Reddening** at the injection site was seen in 27 (14.21%). **Depigmentation of hair** at the injection site was noted by 19 participants (10%). **Pruritis**, or itching, at the injection site was experienced by 15 participants (7.89%). **Twitching** at the injection site was reported by 12 participants (6.32%). **Alopecia**, or hair loss, was reported by 11 participants (5.79%). **Contusions** at the injection site were reported by 8 participants (4.21%). **Lichenification**, a thickening of the skin, was reported by 8 participants (4.21%). **Local hyperesthesia**, an increased sensitivity to touch, was reported by 9 participants (4.74%). **Subcutaneous lesions** were reported by 8 participants (4.21%), represented in figure 17 which was also supplied by FIP Warriors®. **Abscess** formation at the injection site was noted by 5 participants (2.63%). **Necrosis** at the injection site was reported by 2 participants (1.05%). Three separate, single cases (0.53%) reported a **foul odour** at the injection, **oral sores** and **contact reaction** to the acidic GS-like substance. The presence of pain at the injection site was reported by 95 participants, representing 50% of the surveyed cases. This indicates that a considerable number of cats experienced discomfort or pain during the treatment.

Hepatic impairment was seen in 6 cases (3.16%) and renal impairment was seen in 7 (3.68%). 3 cases (1.58%) reported that the treatment may have caused tooth decay. Some notable singular reports (0.53% each) included chin follicular keratinization, cardiac enlargement and arthritis.

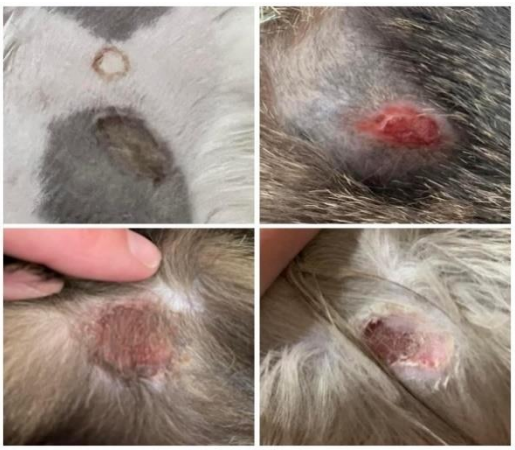


Figure 16. injection site sores (FIP Warriors®, 2023)

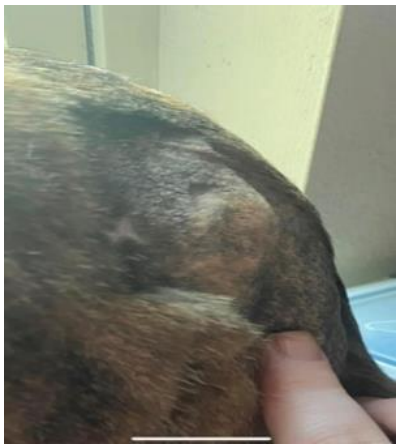


Figure 17. Subcutaneous lesion (FIP Warriors®, 2023)

XXII. Interval for drug therapy to show favourable results

When asked how long it took for noticeable positive effects to begin in these neurological and ocular cases from the start of GS-like therapy, 165 participants (86.24%) noticed positive improvements within only 7 days of treatment. In fact, 34 (17.89%) of owners reported seeing visible improvements within only 24 hours! An additional 12.19% of participants relayed seeing improvements within 8-30 days of the onset of treatment. Only 3 cases (1.57%) reported never seeing any improvement. This can be seen in figure 16, in days.

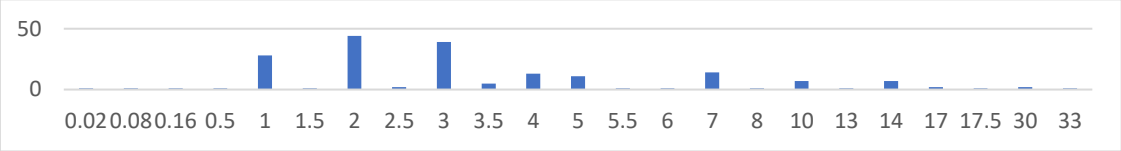


Figure 18. Time in days until positive results seen

XXIII. Health transformations arising from GS

When asked what improvements were seen with GS-like drug therapy, all owners reported a visible improvement in clinical signs very quickly, as shown above. It is important to reiterate that in many of these cases, treatment was still ongoing so the full effect of the the final results may not yet be reflected in these cases. With 179 participants reporting lethargy in their cat 157 (88.40%) reported increased energy levels. In 176 cats with reported loss of appetite, 160 (90.91%) stated their cat had regained it once starting treatment. Weight gain was also a positive outcome for the majority of the 179 cats that had reported weight loss, as 87.1% of them exhibited noticeable increases in weight during their treatment. The overall

condition of the cats also saw substantial progress, with 150 (85.23%) of the 176 cases with poor condition prior to treatment seen improvements. An impressive 132 (83.54%) of the cats 158 with mentioned paralysis, ataxia or loss of balance regained their mobility and exhibited increased activity after treatment. Out of 45 cats with reported fever, it was alleviated in a substantial 41 (91.11%). From the 52 Cats with reported ocular discharge and the 70 with reported nasal discharge, 112 (95.08%) had significantly improved during treatment with GS-like drugs. It was also previously noted that 19 owners seen confusion, aggression or a cognitive change in their cat and its behaviour but after treatment 15 (78.95%) of those cases had returned to normal, improving the cat's mental wellbeing. Before treatment incontinence was referenced in 64 cases, whereas after treatment it was noted that the cats were no longer incontinent in 50 of those cases (78.13%). Finally, out of the 86 cases of ocular FIP recorded in this study, 78 (90.70%) reported that there was ocular improvement during treatment. Recorded examples of these improvements can be seen in figures 19 and 20, where members of FIP Warriors® have shared their ocular FIP progress pictures.

Figure 19. Roman, FIP Warriors® treatment support

Figure 20. Jiji, Nicole Fleming, FIP Warriors® treatment support

Participants of the survey who had completed the entire course of GS-like therapy were asked how they confirmed if their cat was cured following treatment. 53 participants (27.89%) were still ongoing treatment, 4 (2.11%) of participants were still in the observation period and 8 (4.21%) of participants concluded that the cat was not cured as it had died. 125 (65.80%) of the cases had finished treatment and stated that they had concluded that the cats were cured as the biochemistry and haematology blood test parameters returning within the

normal value range, no more clinical signs were evident, 84-day (+) treatment with GS-like therapy had been completed and no signs of relapse during the 84-day observation period following completion of the GS course occurred.

XXIV. Relapse rates

Participants whose cats had completed the GS-like therapy (65.80%) were asked if they experienced a relapse in the observation period. 119 (95.2%) responded ‘no’ and 8 (4.21%) responded ‘yes’. Four of these cases commented on what happened. Case 1. stated that 4 days into the observation period ‘Mr. Wilbur’ became sick again, he was then placed on a much higher dosage of 30mg/kg and has restarted treatment. Case 2. Stated that ‘Tom’ relapsed a whole year after finishing what seemed to be a successful treatment and is currently on 12mg/kg, switching to tablets after 30 days of the injectable form of GS. Everything is now back to normal. Case 3. Stated that ‘Leo’ had wet FIP then in the observation period relapsed with neurological dry FIP. His standard dosage was then doubled and the treatment was continued for 30 more days. Once Leo’s blood work returned to normal, the treatment was stopped and symptoms have gone away since. Finally, case 4. Stated that ‘Semmel’ has relapsed twice. The participant suspects that this was due to partial resistance when taking GS-like therapy orally as even when the dosage was increased, it did not prove helpful. However, when a second antiviral drug which has also shown potential in treating FIP ‘GC376’ was also added to his treatment, he was cured.

XXV. Survival rates

As previously mentioned, 125 participants (65.80%) have completed treatment and have survived neurological or ocular FIP. While 53 (27.89%) cases are still ongoing treatment, the alleviation of clinical signs since starting treatment gives a very positive outlook, with 40 (75.47%) of these cases reporting their cat is back in full health before reaching the end of therapy and the remaining 13 (24.53%) also seeing major improvements. If these cases are included in the survival percentage as they were alive at the time the survey took place, then it rises to 93.68%, although this may be overly optimistic regarding early medical outcomes. In the 8 (4.21%) cases of death, it was noted that mortality often occurred during the initial three weeks of treatment, suggesting that the disease may have progressed too extensively for effective intervention.

XXVI. Long term effects

Some additional comments from owners who completed GS therapy revealed ongoing issues in a small percentage of cases. 4 out of 125 owners (3.2%) reported that their cat had developed kidney failure after, or perhaps, due to treatment. Another 4 owners (3.2%) noted that although their cats' FIPV was cured, the cat still experienced permanent nerve damage. Finally, 2 owners (1.6%) reported ongoing issues with incontinence in their cats.

Discussion

The preceding chapters of this thesis have presented an exploration of FIP, with a distinct focus on its less common neurological and ocular manifestations, as well as its treatment with GS-441524-like drugs. These lesser- studied aspects of FIP pose unique challenges, and this research has aimed to illuminate their complexities.

This study specifically targeted the less common neurological and ocular forms of Feline Infectious Peritonitis (FIP), encompassing cases with distinct characteristics. Among the cases investigated, 54.7% exhibited neurological involvement, 25.79% presented with ocular manifestations, and 19.47% displayed a combination of both neurological and ocular symptoms. Notably, this research diverges from the majority of previous studies, which typically incorporate all forms of FIP into their datasets. As a result, these less common forms have received comparatively less attention and representation in the existing body of research.

The survey received the highest number of responses from France, closely followed by the United States of America, Hungary and other European countries. The initial goal for this study was to evaluate the use of GS-like therapy in neurological and ocular FIP cats in Ireland. However, this proved to be incredibly difficult as the vast majority of responses received from Irish vets conveyed an unknowing of the drug and the great cure rate offered by antiviral drugs such as GS, as well as fear of repercussions for recommendation of unlicensed drugs to owners.

This study found that out of 190 cats, 130 (68.4%) were male, indicating a notable overrepresentation. This trend was common amongst other studies too such as in 2021 by *Jones, S. et al*. where 64.9% of cases were male, as well as in studies by *Riemer et al. 2016*. Additionally, 58.9% of cats were domestic house cats which is surprisingly less than that reported by *Riemer et al., (2016)* where 79% of cats were found to be domestic house cats. Following this, the breeds Maine Coon (11.05%), British Short Hair (5.79%) and Birman (3.68%) were highly represented. It was also found that the vast majority of cases (84.74%) were spayed or castrated as seen in the study by *Garrido-Andersson, L. (2022)* where 81% of cases were neutered. This observation may primarily reflect responsible pet ownership rather than a trend in the underlying pathophysiology of the disease.

A trend was also noted in the age of the cats, with 90% of cases being under the age of 2 years. This finding coincides with *Jones. S. et al., (2021*) where the median age of cats was 1 year and 8 months. It was also discovered that contact with other cats occurred in 87.37%). It is worth noting that 20.5% of participants believe that stress was a predisposing factor in the mutation of FeCoV to FIPV. When it came to other prior illnesses before the onset of FIPV the majority of cats (67.9%) had no previous medical history, and amongst the mentioned prior illnesses, no trend was noticed as a long list of all of the most common ailments of cats was seen throughout the survey. When it came to the discovery of GS-like therapy 50.53% of owners reported being told about it by their own veterinarian. This differs to results found by *Jones, S. et al. (2021*) this was only found in 8.7% of cases. However, in a larger scale study by *Garrido-Andersson, L. (2022)* this trend is supported with 44.9% also being guided towards treatment by their veterinarian.

While almost all of the survey participants did not receive direct assistance from their veterinarians regarding therapy, it was seen that all cases received a presumptive FIP diagnosis. Proof of this via laboratory results such as serum A:G ratio, neutrophils, lymphocytes, monocytes, blood urea nitrogen (BUN) and alanine transaminase (ALT) are typically requested by social media website administrators as prerequisites for commencing GS- like therapy.

84 days was the most commonly observed duration of treatment as recommended by *Pedersen. N.C.* When it came to determining the dosage used in each patient, many owners confused dosage and dose. However, the range shown in correctly answered surveys was between 10mg/kg- 54mg/kg with a median of 15mg/kg as the starting dosage, differing to that of FIP without neurological or ocular involvement which has a much lower average starting dosage of 4-6mg/kg *(Pedersen. N.C, 2021*). It was also seen that approximately 55% of cases, which were mainly neurological FIP, needed to increase the dosage during treatment due to lack of improvement or worsening clinical signs. This is because of the efficacy of the BBB. Pedersen recommends daily increases of 2-5mg/kg for a minimum of 28 days in these instances.

When it came to treatment related complications 46.2% of cases reported injection site reactions such as sore, reddening, depigmentation of hair, pruritis and more. This is similar to the 43.4% reported by *Garrido-Andersson, L. (2022*). However only 50% of cases reported pain at the injection site in this study compared to 70.3% reported by Garrido. This

could be due to the difference in question wording comparing pain at the injection site in general versus during injection of the acidic substance.

A notable improvement was seen in the neurological and ocular FIP cases during treatment with GS-like drugs within 7 days of treatment in 86.24% of cases. These results are common and it is stated by FIP Warriors® in many sources for owner information that improvement is generally seen within 48-72 hours of beginning GS. This aligns with the 17.89% of owners who seen improvements in less than 24 hours.

It must be mentioned that only 4.2% of cases suffered from a relapse in the observation period. This relapse rate does not seem to be any higher when compared with non-neurological or non- ocular cases, as the relapse rate reported by *Jones, S. et al. (2021)* was a significantly higher, 12.7% but was a lower 1.2% in the study by *Garrido-Andersson, L. (2022)* showing no conclusive pattern.

With 65.80% participants in the survey having completed treatment and being out of the observation period and 93.68% having positive results up to the time of the survey, and only 4.2% of cases ending in fatalities, it can be concluded that GS-like therapy has a profound effect and is very effective in treating neurological and ocular FIP since without therapy, all cats would have succumbed to the lethal disease.

This study is subject to several limitations that warrant consideration. One significant limitation is the reliance on cat owners, rather than medical professionals, for data collection. While this approach provides valuable insights into real-world experiences, it introduces the potential for bias. Notably, many participants were associated with cats that had successfully survived treatment with GS-like therapy and may primarily attract individuals with a strong interest in the subject matter, potentially limiting the diversity of responses which could lead to a lack of representation from owners whose cats did not survive the treatment. This selection bias could impact the generalizability of the findings. Additionally, the use of an online survey format poses challenges, such as the potential for misinterpretation of questions, despite efforts to clarify and correct as necessary. These limitations should be taken into account when interpreting the results of this study and underscore the need for future research to address these potential shortcomings.

Conclusion

In conclusion, the research in this thesis confirms GS-441524's efficacy in treating cats with neurological and ocular Feline Infectious Peritonitis (FIP). Data from clinical trials, case studies, and experimental treatments consistently show positive outcomes, including symptom relief, increased survival rates, and enhanced quality of life for affected feline patients. This highlights GS-441524 as a valuable therapeutic option for a historically challenging veterinary condition.

With compelling evidence of its effectiveness, GS-441524 should be considered for legal approval and made readily available to veterinarians and pet owners. The current lack of approved FIP treatments, especially for neurological and ocular forms, leaves limited options and often leads to devastating outcomes. Making GS-441524 accessible can revolutionize FIP treatment, offering hope and relief to countless feline companions and their caregivers.

However, it's crucial to emphasize that further research and rigorous testing are essential to ensure the treatment's safety and efficacy in broader clinical use, including addressing potential side effects, dosing regimens, and long-term effects. Collaborative efforts between researchers, pharmaceutical companies, and regulatory bodies are vital for responsible development and approval of this promising treatment. In conclusion, the approval and availability of GS-441524 have the potential to transform the lives of countless cats and their owners, warranting continued research and expedited regulatory processes to make this crucial treatment accessible.

Abstract in English

Feline infectious peritonitis (FIP) is a lethal disease in cats, resulting from a mutation of the Feline Coronavirus, occurring in approximately 1-2% of cases. FIP manifests in two forms: wet and dry, occasionally accompanied by neurological or ocular symptoms. Recently, pet owners have turned to GS-441524, an unapproved antiviral nucleoside analogue, to treat their FIP-afflicted cats, reporting remarkable outcomes. No legally available drugs have shown success in FIP treatment, but a significant issue is the lack of scientific documentation due to the sourcing of GS-441524 from illicit markets.

This study aimed to systematically evaluate the use of unlicensed GS-441524-like treatment in cats suspected of having neurological and ocular FIP, a previously incurable ailment. An online survey was conducted among members of various large social media support groups and GS-441524-like drug distribution networks. The survey targeted individuals who had treated their cats with GS-441524, who had neurological or ocular FIP, for a minimum of 84 days. Among the 226 survey responses received, 190 met the inclusion criteria.

A majority of respondents (around 87%) reported significant improvements in their cats' health within a week of starting the therapy. At the time of the survey, about 96% of cats were still alive, with approximately 61% considered cured and an additional 35% under observation during the 84-day period. A small portion (4%) experienced FIP symptom relapses, and the same percentage did not survive despite receiving GS-441524-like therapy. Complications were mainly associated with owner-administered subcutaneous injections of the acidic GS-441525-like therapy, leading to issues like pain, injection site injuries, and kidney damage.

It's essential to acknowledge the limitations of this study, including reliance on owner-reported data alongside input from medical professionals and an inability to verify the composition of unapproved pharmaceuticals. Nevertheless, valuable insights can be gained from the experiences shared by these cat owners. Although unconventional and not without medical and legal risks, based on owner testimonials, at-home GS-441524-like therapy appears to offer potential benefits for cats suspected of having FIP.

Absztrakt Magyarul

A macskákban előforduló fertőző hasmenéses peritonitis (FIP) egy halálos betegség, amely a macska koronavírus mutációjából ered, és az esetek kb. 1-2%-ában fordul elő. A FIP két formában jelentkezhet: nedves és száraz, néha idegrendszeri vagy szemészeti tünetek kíséretében. Az utóbbi időben a háziállat-tulajdonosok a GS-441524 nevű, engedély nélküli antivirális nukleozid analógot kezdték alkalmazni FIP-ben szenvedő macskáiknál, és rendkívüli eredményekről számoltak be, de komoly probléma az orvosi dokumentáció hiánya, ami a GS-441524 beszerzési forrásainak tiltott jellegéből adódik. Legálisan elérhető gyógyszer eddig nem bizonyult hatékonynak a FIP kezelésében.

Ez a tanulmány arra irányult, hogy elemezze a nem engedélyezett GS-441524-szerű kezelés használatát azon macskáknál, akiknél idegrendszeri és szemészeti FIP gyanúja merült fel, egy eddig gyógyíthatatlannak tartott betegség esetében. Egy online felmérést végeztünk el különböző nagy közösségi média támogató csoportok és GS-441524-szerű gyógyszerterjesztési hálózatok tagjai között. A felmérés azokra a macskatulajdonosokra összpontosított, akik macskáánál idegrendszeri vagy szemészeti FIP gyanúja merült fel és az állatnál legalább 84 napig tartó GS-441524 kezelésre került sor. A 230 beérkezett válaszból 190 felelt meg a beválogatási kritériumoknak.

A válaszadók többsége (kb. 87%) azt nyilatkozta, hogy macskáik egészségi állapota jelentős javulást mutatott egy hét elteltével a kezelés megkezdése után. A felmérés idején a macskák mintegy 96%-a még életben volt, és körülbelül 61%-ukat már gyógyultnak tekintették, további 35%-ukat pedig további megfigyelés alatt tartották a kezelést követő 84 napos időszak alatt. Egy kis részük (4%) FIP tünetek visszaesését tapasztalta, és ugyanennyi százalékuk nem élt túl annak ellenére sem, hogy GS-441524-szerű terápiát kapott. A kezelés mellékhatásai főként a savas PH-jú injekciós készítmény tulajdonos által adott bőralatti injekció beadásával voltak összefüggésben, olyan problémákat okozva, mint a fájdalom, az injekcióhelyi sérülések és a vese károsodása.

Fontos megjegyezni ennek a tanulmánynak a korlátait, ideértve azt hogy tulajdonosok által bejelentett adatokra támaszkodik, állatorvosok és az engedély nélküli gyógyszerek összetételének ellenőrizhetetlensége mellett. Mindazonáltal értékes tanulságok vonhatók le ezekből a tapasztalatokból. Bár szokatlan és nem mentes az orvosi és jogi kockázatoktól, az egyéni tapasztalatok alapján úgy tűnik, hogy az otthoni GS-441524-szerű terápia jelentős előnyöket nyújthat az FIP idegrendszeri formájában szenvedő macskák számára.

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I hereby confirm that I am familiar with the content of the thesis entitled

Literature review and questionnaire-based retrospective study: The treatment of Neurological and ocular FIP with GS-441524

..... written by Niamh Maria O'Shaughnessy

(student name) which I deem suitable for submission and defence.

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DECLARATION

I hereby declare that the thesis entitled Literature review and questionnaire-based retrospective study: The Treatment of Neurological and Ocular Feline Infectious Peritonitis with The Nucleoside Analogue GS-441524 is identical in terms of content and formal requirements to the TDK research paper submitted in 2023 (year).
Date: 06/11/2023

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Thesis progress report for veterinary students

Name of student: Niamh Maria O' Shaughnessy

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Consultation – 1st semester

	Timing			Topic / Remarks of the supervisor	Signature of the supervisor
	year	month	day		
1.	2023	02.	07.	Discussion of the topic	PTV.
2.	2023.	04.	11	Discussion literature and questionnaire	PTV.
3.	2023.	07.	06.	First draft of lit review	PTV.
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Grade at the end of the first semester: ……

Consultation – 2nd semester

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1.	2023.	09.	04.	First corrections	PTV.
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3.	2023.	10	15.	Final ~~topic~~ version	PTV.
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