# Unlicensed antiviral treatment with GS-441524: How are clinicians approaching feline infectious peritonitis in primary care practices?

A. Schlachet[1], E. Moillen[1], S. Schuller[1], A. Carranza Valencia[1]

[1]Division of Small Animal Internal Medicine, Department of Clinical Veterinary Science, Vetsuisse Faculty, University of Bern, Switzerland

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## Nicht zugelassene antivirale Behandlung mit GS-441524: Wie gehen Tierärzte in der medizinischen Grundversorung mit der infektiösen Peritonitis bei Katzen um?

Die weltweite Verfügbarkeit von GS-441524 zur Behandlung der infektiösen Peritonitis bei Katzen (FIP) hat in den letzten Jahren zugenommen. Es existieren jedoch nur wenige Daten, wie Tierärztinnen und Tierärzte in der Grundversorgung die Krankheit diagnostizieren. Ziel dieser Studie war es, den diagnostischen Ansatz für FIP in der Primärversorgung zu evaluieren und die Ergebnisse zwischen exsudativen und nicht-exsudativen Formen zu vergleichen.

Es wurde eine retrospektive Analyse anhand eines Datensatzes von 243 Katzen durchgeführt, die in der Westschweiz mit dem nicht zugelassenen GS-441524 behandelt wurden und über eine Social-Media-Plattform erfasst wurden. Alle Katzen hatten eine mindestens 12-wöchige Behandlung abgeschlossen.

Die demografischen Daten stimmten mit früheren Berichten überein. Exsudative und nicht-exsudative FIP waren gleichermassen vertreten. Zu den häufigsten Beschwerden gehörten Hyporexie/Anorexie (70 %; 166/236), Gewichtsverlust (63 %; 149/236) und Lethargie (59 %; 140/236). Hyporexie/Anorexie trat häufiger bei Katzen mit exsudativer FIP auf (P < 0,001). Zu den häufigsten diagnostischen Tests gehörten ein vollständiges Blutbild und die Biochemie (92 %; 224/243), Serum-FCoV-Antikörpertiter (28 %; 69/243), FCoV-PCR (28 %; 69/243), Serumamyloid A (SAA) (27 %; 65/243), Serumproteinelektrophorese (20 %; 48/243) und abdominaler Ultraschall (19 %; 46/243). Katzen mit exsudativer FIP wurden häufiger einem FCoV-PCR-Test unterzogen als Katzen mit nicht-exsudativer FIP (P < 0,001). Umgekehrt lagen bei Katzen mit nicht-exsudativer FIP häufiger FCoV-Titer vor (P < 0,001). Zu den häufigsten pathologischen Laborbefunden gehörten Hyperglobulinämie (80 %; 179/223), erhöhte SAA-Werte (78 %; 51/65),

## Summary

The global availability of GS-441524 for treating feline infectious peritonitis (FIP) has increased in recent years, yet little data is available about how primary care veterinarians diagnose the disease. This study aimed to evaluate the diagnostic approach to FIP in primary care practices and compare findings between effusive and non-effusive forms.

Retrospective analysis was conducted using a dataset of 243 cats treated with unlicensed GS-441524 in Western Switzerland, obtained via a social media platform, all of which completed a minimum of 12-weeks treatment.

Demographics were consistent with previous reports. Effusive and non-effusive FIP forms were equally represented. Most common presenting complaints included hyporexia/anorexia (70 %; 166/236), weight loss (63 %; 149/236), and lethargy (59 %; 140/236). Hyporexia/anorexia was more common in cats with effusive FIP (P <0,001). Most common diagnostic tests included complete blood count and biochemistry (92 %; 224/243 each), serum FCoV antibody titers (28 %; 69/243), FCoV PCR (28 %; 69/243), serum amyloid A (SAA) (27 %; 65/243), serum protein electrophoresis (20 %; 48/243), and abdominal ultrasound (19 %; 46/243). Cats with effusive FIP were more likely to undergo FCoV PCR testing compared non-effusive FIP cats (P <0,001). Conversely, cats with non-effusive FIP had more frequently FCoV titers available (P <0,001). Most common laboratory abnormalities included hyperglobulinemia (80 %; 179/223), increased SAA (78 %; 51/65), anemia (55 %; 124/224), hyperproteinemia (54 %; 123/227), and albumin:globulin ratio <0,4 (53 %; 120/225). Hyperproteinemia was significantly more common in cats with non-effusive FIP (67 %; 76/114; P <0,001), whereas hypoalbuminemia was significantly more frequent in cats with effusive FIP (39 %; 43/111; P <0,001).

These results demonstrate that decisions to treat cats with GS-441524 in primary care practices relies on a presump-

Anämie (55 %; 124/224), Hyperproteinämie (54 %; 123/227) und ein Albumin-Globulin-Verhältnis < 0,4 (53 %; 120/225). Hyperproteinämie trat signifikant häufiger bei Katzen mit nicht-exsudativer FIP auf (67 %; 76/114; P < 0,001) auf, während Hypoalbuminämie signifikant häufiger bei Katzen mit exsudativer FIP auftrat (39 %; 43/111; P < 0,001).

Diese Ergebnisse zeigen, dass die Entscheidung, Katzen in der Grundversorgung mit GS-441524 zu behandeln, auf einer Verdachtsdiagnose mit minimalen diagnostischen Tests beruht. Es sollten Kriterien definiert werden, um Fälle zu identifizieren, in denen Bestätigungstests, wie RT-PCR für FCoV, unerlässlich sind, um Fehldiagnosen und den unsachgemässen Einsatz von Virostatika zu vermeiden.

**Schlüsselwörter:** Katze, Coronavirus, exsudativ, trocken, FCoV, FIP

tive diagnosis with minimal diagnostic testing. Criteria should be defined to identify cases where confirmatory testing, such as RT-PCR for FCoV, is essential, to prevent misdiagnoses and inappropriate use of antivirals.

**Keywords:** cat, coronavirus, effusive, dry, FCoV, FIP

## Introduction

Antiviral drugs such as GS-441524 have recently demonstrated high efficacy in the treatment of feline infectious peritonitis (FIP).[2,4,8,9,17,22] GS-441524 is now licensed for veterinary use in several countries, including the United States, Canada, Australia, and the United Kingdom. However, access remains largely restricted in many others, such as Switzerland, where it is limited to academic research or obtained through illegal, unregulated sources. Given the increasing global accessibility of GS-441524, it is crucial for veterinarians to ensure an accurate diagnosis of FIP before initiating treatment, in order to prevent overuse or misuse of antiviral agents. Moreover, the excessive use of antivirals may contribute to the emergence of antiviral resistance, a phenomenon already well-documented in human medicine.[1,12,19,20]

Diagnosing FIP can be challenging, especially in cases of non-effusive FIP.[17,22] Although guidelines are available to assist practitioners in identifying suspected cases of FIP, they rely on a multitude of diagnostic tests to establish a high index of suspicion.[15,18] Nevertheless, comprehensive diagnostic workups are not always feasible due to financial limitations, restricted test availability, and time constraints. Little data is available regarding the diagnostic tests performed in primary care practices, where most FIP cats are treated or will be treated once antivirals get licensed. Documenting the diagnostic approach of primary care veterinarians could help identify major discrepancies between current recommendations and daily practice, enabling appropriate adjustments. Therefore, the primary aim of this study was to assess the diagnostic approach used by primary care practitioners in cats with suspected FIP, based on a cohort of cats treated with unlicensed GS-441524 in Switzerland. Additional aims were to evaluate the clinical and clinicopathological response to treatment, compare the diagnostic approaches and findings between effusive and non-effusive FIP cases, and document treatment protocols.

## Materials and methods

### Study population

A dataset of cats treated for FIP with unlicensed GS-441524 in Western Switzerland between September 2020 and July 2023 was retrospectively analyzed. During this period, GS-441524 was not licensed for use in Switzerland, and treatment in veterinary practices, as described in this report, occurred outside the current legal framework. Because of its retrospective nature, this study was exempt from formal ethical approval. This dataset was sourced through the administrator of a public social media group on Meta's Facebook platform and contained cases attending mainly primary care practices. It included an Excel table with demographic data, FIP form, antiviral brand and dose, and a link to a Facebook post for each cat. These posts contained information on clinical signs, diagnostic work-up, treatments, and follow-up. In the Excel table, cats were classified as «under treatment», in «observation period», «cured» or «deceased». For ethical reasons, online documentation about deceased cats was erased, but comments on cause of death or alternative diagnoses were recorded in the Excel table.

### Treatment overview

Cats were treated with unlicensed GS-441524 sourced from Hong Kong. The treatment protocol, advised by the Facebook group moderator, consisted of 12-week of GS-441524 administered subcutaneously (SC) or orally (PO), followed

by a 12-weeks observation period. Starting doses were 6-7 mg/kg SID for effusive/non-effusive FIP, 8 mg/kg SID for ocular FIP, and 10 mg/kg SID for neurological FIP. Follow-up examinations were recommended every four weeks during treatment and every six weeks during the observation period. Cats clinically healthy after both phases were deemed cured.

### Case recruitment and data collection

Included cats belonged to the «cured», «observation period,» or «deceased» categories. Cats still under treatment and those that died from other diseases were excluded. By the time of data analysis, all cats in the observation period were reclassified as cured. Final categorization was therefore limited to cured or deceased cats. Due to lack of information on deceased cats, diagnostic approaches and comparison between effusive and non-effusive FIP were only assessed in cured cats. Cured cats deemed unlikely to have FIP, or lacking information on both clinical signs and laboratory findings, were further excluded.

Collected data at diagnosis included: demographics (age, sex, weight and breed), clinical signs, diagnostic tests (complete blood count [CBC], biochemistry, serum amyloid A [SAA] concentration, serum protein electrophoresis [SPE], FCoV titers, FCoV PCR results, thoracic radiographs, abdominal ultrasound, cytology findings, effusion analysis), and dose of GS-441524. At each follow-up examination, clinical evolution, laboratory findings (CBC, biochemistry, SAA concentration, SPE), and treatment adjustment were registered.

### FIP Form

Cats documented with pleural or abdominal effusion were classified as having effusive FIP, and those without as having non-effusive FIP. Both groups were further categorized based on the documentation of neurological signs, ocular signs, or both.

### Diagnosis of FIP

The 2022 AAFP/EveryCat FIP Diagnosis Guidelines and the algorithm tools from the European Advisory Board for Cat diseases were used to review and categorize the diagnosis of FIP by two of the authors AS and ACV, as previously described.[15,17,18] Cats were classified as: (1) very likely to have FIP if they had consistent signalment, clinical signs, laboratory findings and identification of FCoV RNA by RT-PCR; (2) highly suspicious of having FIP if they had consistent signalment, clinical signs, laboratory findings, without confirmed presence of FCoV RNA by RT-PCR or FCoV antigen by immunostaining; (3) confirmed to have FIP if they had consistent signalment, clinical signs, laboratory findings, with confirmed presence of FCoV antigen by immunostaining.

### Statistical analysis

Demographics, clinical signs, and laboratory findings were summarized by descriptive statistics. Statistical tests were performed to compare clinical and clinicopathological findings of cats with effusive and non-effusive FIP. Qualitative variables were compared using the Chi-square test (or Fisher's exact test when the assumptions for the Chi-square test were not met). Mann-Whitney U test was used to compare quantitative variables. Results were considered statistically significant when the p-value was less than 0,05. The Bonferroni correction was applied for multiple comparisons.

## Results

### Case selection

Data of 344 cats treated with unlicensed GS-441524 for suspected FIP were available. The following cats were excluded: 35 cats still under treatment, 16 cats that died from non-FIP causes, 7 cats lacking both clinical and laboratory data, and one cat deemed unlikely to have FIP. The final study population included 243 cured cats and 42 cats with presumed FIP-related death. Further analysis focused on the cured group.

### Medical records

Table 1 shows the demographic data for all cured cats and according to the FIP form. No significant differences were found between the two groups. Most cats were non-pedigree (65 %; 159/243). Overall, 18 breeds were represented, including: 13 Maine Coon, 12 Birman, 10 British Shorthair, nine Bengal, six Persian, five Sphynxes, five Abyssinian, four Oriental, four British Longhair, three Siberian, three Singapura, two Ragdoll, two Russian Blue, two Korat and one each of Siamese, Burmese, Norwegian Forest Cat, and American Shorthair.

Clinical signs at diagnosis are shown in Table 2. Fifty percent (122/243) of cats had effusive FIP and 50 % (121/243) non-effusive FIP. Seven cats lacked detailed clinical signs but had laboratory results and documentation of the FIP form. The most commonly reported clinical signs were hyporexia/anorexia (70 %; 166/236), weight loss (63 %; 149/236), lethargy (59 %; 140/236) and fever (54 %; 128/236). Few cats were reported to have gastrointestinal symptoms or icterus. Neurological and ocular signs were reported in 12 % (29/243) and 14 % (35/243) of cats, respectively (detailed signs in Table 3).

Among effusive FIP cases, 41 % (100/243) had abdominal effusion, 9 % (23/243) had pleural effusion, and one cat had both. Hyporexia was significantly more frequent in cats with effusive FIP (P <0,001), while neurological and ocular signs were more common in non-effusive FIP (P =0,002 and P <0,001, respectively). The remaining clinical signs showed no significant differences between groups.

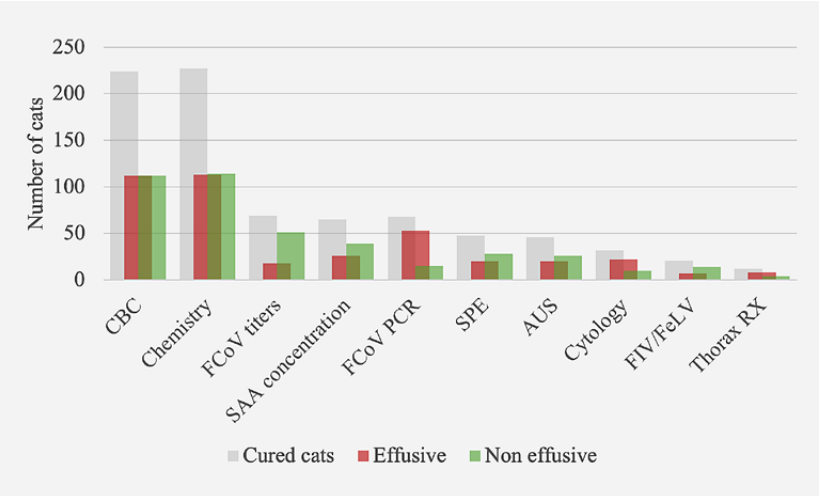


**Figure 1:** Diagnostic tests performed at diagnosis in all cured cats and according to the effusive and non-effusive forms of feline infectious peritonitis
Abbreviations: Ab, antibody; AUS, abdominal ultrasound; SPE, serum protein electrophoresis

## Diagnostic approach

Available diagnostic tests at diagnosis are summarized in Figure 1. CBC (92 %; 224/243) and biochemistry (92 %; 224/243) were the most common, followed by FCoV serology (28 %; 69/243), FCoV PCR (28 %; 68/243), SAA concentration (27 %; 65/243), and SPE (20 %; 48/243). Imaging was reported in 22 % (54/243) of cats and included abdominal ultrasound (19 %; 46/243) and thoracic radiographs (5 %; 12/243). Cytology reports were available in 13 % (31/243) of cases, mainly from effusion samples (70 %; 21/31). Other sampled sites included abdominal lymph nodes (n = 4), kidneys (n = 3), spleen (n = 2), liver (n = 2), abdominal mass (n = 1), and colon (n = 1). No reports included FCoV immunocytochemistry or immunohistochemistry.

Cats with effusive FIP more frequently had PCR results available (43 %; 53/122) compared to cats with non-effusive FIP (13 %; 15/120) (P <0,001). Conversely, non-effusive FIP cases more frequently had FCoV titers available (74 %; 51/69) compared to effusive FIP cases (26 %; 18/69) (P <0,001).

**Table 1:** Demographics at diagnosis in all cured cats and according to the effusive and non-effusive forms of feline infectious peritonitis

| | All cats (n=243) | Effusive FIP (n=122) | Non-Effusive FIP (n=121) | P-value[1] |
|---|---|---|---|---|
| **Median age (range)** | 11 months (2-240) | 10 months (3-240) | 12 months (2-168) | 0,098 |
| **Male** | 64 % (155/241) | 65 % (78/120) | 64 % (77/121) | 0,825 |
| **Non-pedigree** | 65 % (159/243) | 62 % (76/122) | 69 % (83/121) | 0,301 |
| **Median weight (range)** | 3,0 kg (0,86-7,5) | 3,0 kg (0,86-7,5) | 3 ,0 kg (1,2-5,8) | 0,390 |

Abbreviations: [1] P-value: statistical comparison between effusive and non-effusive FIP groups; n: total number of cats

**Table 2:** Clinical signs at diagnosis in all cured cats and according to the effusive and non-effusive forms of feline infectious peritonitis

| Clinical signs | Total % (n/total) | Effusive FIP % (n/total) | Non-effusive FIP % (n/total) | P-value[1] |
|---|---|---|---|---|
| **Hypo/Anorexia** | 70 (166/236) | 73 (88/120) | 67 (78/116) | <0,001* |
| **Weight loss** | 63 (149/236) | 58 (69/120) | 69 (80/116) | 0,068 |
| **Lethargy** | 59 (140/236) | 62 (74/120) | 57 (66/116) | 0,456 |
| **Fever** | 54 (128/236) | 56 (67/120) | 53 (61/116) | 0,617 |
| **Diarrhea** | 9 (21/236) | 7 (8/120) | 11 (13/116) | 1 |
| **Vomiting** | 6 (13/236) | 4 (5/120) | 7 (8/116) | 1 |
| **Icterus** | 3 (6/236) | 3 (3/120) | 3 (3/116) | 1 |
| **Dyspnea** | 3 (7/236) | 6 (7/120) | 0 (0/116) | 0,014 |
| **Ocular signs** | 14 (35/243) | 5 (6/122) | 24 (29/121) | <0,001* |
| **Neurological signs** | 12 (29/243) | 6 (7/122) | 18 (22/121) | 0,002* |
| **Abdominal effusion** | 41 (100/243) | 82 (100/122) | – | – |
| **Pleural effusion** | 9 (23/243) | 19 (23/122) | – | – |

Abbreviations: [1] P-value: statistical comparison between effusive FIP and non-effusive FIP groups; *significant difference between effusive FIP and non-effusive FIP groups; n: absolute number of cats presenting with the clinical sign; total: total number of observations

## Laboratory findings at diagnosis

Table 4 summarizes laboratory findings at diagnosis. The most common laboratory abnormalities included hyperglobulinemia (80 %; 179/223) and increased SAA concentration (78 %; 51/65). Around half of the cats had anemia (55 %; 124/224), hyperproteinemia (54 %; 123/227), and an albumin:globulin (AG) ratio <0,4 (53 %; 120/225). Hyperproteinemia was significantly more frequent in cats with non-effusive FIP, while hypoalbuminemia was more frequent in cats with effusive FIP (both P < 0,001). No other laboratory differences were statistically significant.

FCoV PCR was positive in 84 % (52/62) and negative in 16 % (10/62); results were unavailable for 6/68 cats.

**Table 3:** Neurological and ocular signs at time of diagnosis

| Ocular signs | Total % (n/total) |
|---|---|
| Uveitis | 60 % (21/35) |
| Anisocoria | 17 % (6/35) |
| Mydriasis | 11 % (4/35) |
| Blindness | 6 % (2/35) |
| Fibrin deposit | 6 % (2/35) |
| Opacity | 6 % (2/35) |
| Retinal detachment | 3 % (1/35) |
| Glaucoma | 3 % (1/35) |
| Chorioretinitis | 3 % (1/35) |
| Hyphema | 3 % (1/35) |
| **Neurological signs** | **Total % (n/total)** |
| Ataxia | 76 % (22/29) |
| Head shivering | 14 % (4/29) |
| Seizures | 10 % (3/29) |
| Incontinence | 7 % (2/29) |
| Spasms of the distal limbs | 7 % (2/29) |
| Disorientation | 7 % (2/28) |

Abbreviations: n: absolute number of cats with the clinical sign; total: total number of observations

**Table 4:** Laboratory findings at diagnosis in all cured cats and according to the effusive and non-effusive forms of feline infectious peritonitis

| Laboratory findings | All cured cats % (n/total) | Effusive FIP % (n/total) | Non-effusive FIP % (n/total) | P-value[1] |
|---|---|---|---|---|
| Anemia | 55 % (124/224) | 58 % (65/113) | 53 % (59/111) | 0,106 |
| Neutrophilia | 44 % (97/221) | 48 % (54/113) | 40 % (43/108) | 0,233 |
| Leukocytosis | 35 % (78/224) | 37 % (42/113) | 32 % (36/111) | 0,457 |
| Lymphopenia | 14 % (32/222) | 17 % (19/113) | 12 % (13/109) | 0,300 |
| Hyperglobulinemia | 80 % (179/223) | 77 % (85/111) | 84 % (94/112) | 0,168 |
| Elevated SAA | 78 % (51/65) | 85 % (22/26) | 74 % (29/39) | 0,324 |
| Hyperproteinemia | 54 % (123/227) | 42 % (47/113) | 67 % (76/114) | <0,001* |
| AG <0.4 | 53 % (120/225) | 49 % (54/111) | 59 % (66/112) | 0,124 |
| Hyperbilirubinemia | 35 % (72/203) | 43 % (44/102) | 28 % (28/101) | 0,022 |
| Hypoalbuminemia | 29 % (64/223) | 39 % (43/111) | 19 % (21/112) | <0,001* |
| Elevated ALT | 11 % (22/203) | 8 % (8/105) | 14 % (14/98) | 0,127 |
| Positive FCoV PCR | 84 % (52/62) | 83 % (40/48) | 86 % (12/14) | 1 |
| Positive FCoV titers | 94 % (65/69) | 89 % (16/18) | 96 % (49/51) | 1 |
| Negative FIV/FeLV | 90 % (19/21) | 100 % (7/7) | 86 % (12/14) | 0,533 |

Abbreviations: [1] P-value: statistical comparison between effusive and non-effusive FIP groups; *significant difference between effusive and non-effusive FIP groups; AG: albumin:globulin ratio; n: absolute number of cats with the mentioned laboratory abnormality; total: total number of observations

## Clinical and laboratory findings at follow-up examinations

Clinical improvement was assessed through brief comments on general well-being and changes in body weight at each follow-up. Figures 2 and 3 illustrate a progressive decline in laboratory abnormalities over time. At week 4, hyperglobulinemia (53 %; 91/171), hyperproteinemia (28 %; 52/186), anemia (14 %; 25/182), elevated SAA concentrations (14 %; 21/153), and leukocytosis (14 %; 25/182) were the most frequently observed. By week 8, hyperglobulinemia (30 %; 45/152), hyperproteinemia (12 %; 19/158), and elevated SAA (11 %; 14/133) remained the most common. At week 12, only hyperglobulinemia (24 %; 42/177) and elevated SAA (11 %; 19/174) were still among the most prevalent. By week 24, all parameters had normalized in most cats, with a few remaining cases of elevated SAA (13 %; 13/102), hyperproteinemia (8 %; 9/119), and hyperglobulinemia (5 %; 5/91).

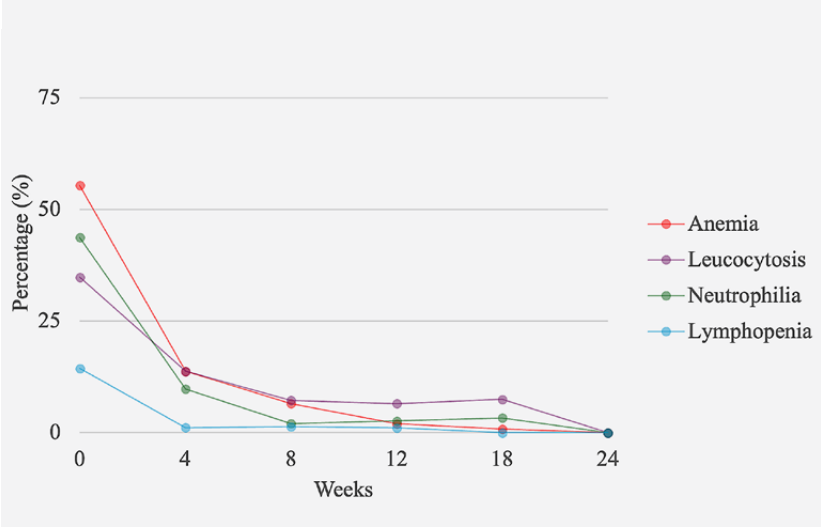


**Figure 2:** Evolution of the percentage of cats having hematologic abnormalities at diagnosis and during follow-up examinations

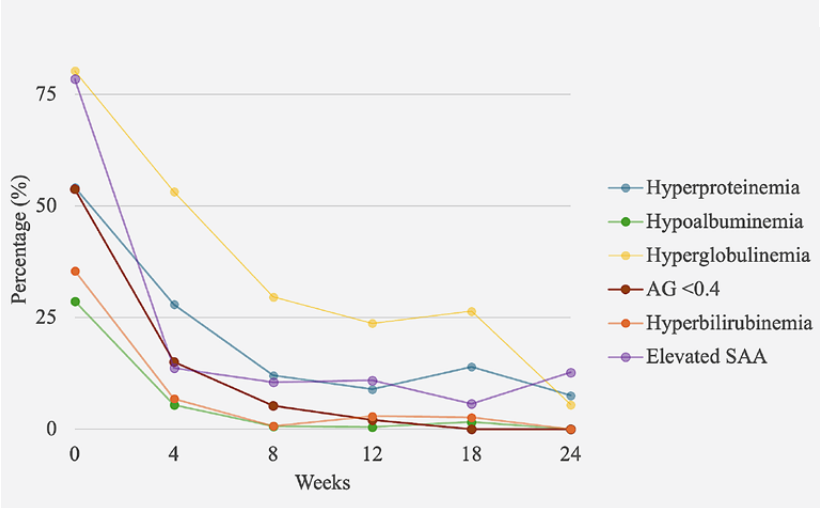


**Figure 3:** Evolution of the percentage of cats having biochemical abnormalities at diagnosis and during follow-up examinations

## Diagnosis of FIP

Based on signalment, clinical signs, and laboratory findings, FIP diagnosis was classified as very likely in 21 % (52/243) and highly suspicious in 79 % (191/243) of cases. No diagnosis was confirmed by immunocytochemistry or immunohistochemistry.

## Treatment protocols

Most cured cats were treated for 12 weeks with GS-441524 at 6-11 mg/kg SID (81 %; 197/243). Cats with prolonged therapy (19 %; 46/243) had a median treatment duration of 14 weeks (range: 13-27 weeks). Most cats (57 %; 139/243) were treated exclusively with oral medication. Approximately 25 % (59/243) of the cats had a dose increase within the first four weeks, and after the four-week follow-up (65/243). Four cats relapsed during the observation period (at weeks one, four, and six after stopping treatment). Relapses included recurrence of symptoms (lethargy, weight loss, hyporexia), pleural effusion in two cats, and neurological symptoms in one. Three cats were treated again with GS-441524 at doses 5 mg/kg higher than initially. One cat was switched to molnupiravir. All relapsed cats were reported to be cured after completion of the second treatment. Follow-up duration ranged from 711 to 1747 days for all cured cats.

## Mortality cases

Fifty-eight cats died during the study period, with 16 deaths attributed to causes unrelated to FIP. These included two cases of neoplasia (lymphoma, intestinal tumor), two car accidents, one related to orthopedic surgery, ten cases of euthanasia due to other unspecified conditions, and one case of respiratory arrest following pill ingestion.

For the remaining 42 cats that were considered to have a FIP-related death, the median age was 12 months (range: 3-228 months) and the median weight was 2,7 kg (range: 1-5,2 kg). Breed and sex information were unavailable for most cats. Effusive FIP was most frequently reported (76 %; 32/42). Neurological and ocular signs were reported in 17 % (7/42) and 5 % (2/42) of cats, respectively. The median treatment duration was six days (range: 1-140 days), with a median dose of 6 mg/kg (range: 6-12 mg/kg) given orally in 45 % (19/42) of cases. Reported causes of death included respiratory distress (24 %; 10/42) and neurological deterioration (7 %; 3/42) but were unknown in 69 % (29/42) of cases.

## Discussion

The results of this study indicate that, in this cohort of cats, a presumptive diagnosis of FIP and the decision to treat with GS-441524 was primarily based on demographics, clinical signs, hematological and biochemical findings. Additional diagnostic tests, including confirmatory tests for FCoV, were reported in less than one third of cases. Nonetheless, the consistency of findings and treatment response, which closely align with previously published findings, strongly support that this population indeed had FIP.[2,8,9,13,17,21]

Gold standard for the definitive diagnosis of FIP remains histopathology in combination with immunohistochemistry (IHC), which allows identification of FCoV within characteristic lesions.[15,18] Due to its invasive nature, tissue sampling is mainly performed post-mortem. Alternatively, RT-PCR testing on appropriate samples shows high sensitivity and specificity in identifying FCoV.[5,10,15] A combination of consistent history, signalment, clinical signs and clinicopathological findings, including identification of FCoV by RT-qPCR, is often recommended for the diagnosis of FIP.[15,18] In the present study, only 28 % of cases had a FCoV PCR report available, mostly on effusion samples (80 %). Limited use of PCR testing might reflect potential barriers such as limited access to specialized laboratories, challenges in obtaining samples (FNAs, CSF and aqueous humor), financial constraints, concerns about delaying treatment, or variability in clinician training and awareness regarding FIP diagnosis. At the same time, it reflects the possibility to establish a high suspicion of FIP mainly based on demographics, clinical signs and laboratory findings.[6] As PCR testing is unlikely to increase significantly in primary care practice, especially for non-effusive FIP cases, future guidelines for diagnosis and treatment should include clear indications for PCR testing.

Cytology reports were less frequently available than PCR reports, despite being more accessible, more affordable, and requiring the same sampling process. Most cats with cytology reports also had PCR reports, suggesting that these diagnostic methods are often used in tandem rather than as alternatives. Cytological analysis is a cornerstone in the diagnosis of FIP, especially in excluding diseases with similar presentations (e.g. septic peritonitis, pyothorax, lymphoma).[15,18] Further efforts should be directed toward increasing awareness among practitioners of its value in the diagnostic approach to FIP to avoid misdiagnoses and an improper use of antiviral drugs, particularly in non-straight-forward cases.

FCoV antibody titers were reported as often as PCR testing and were more frequently performed in non-effusive FIP cases. However, FCoV serology is of limited value in the diagnosis of FIP and can only offer meaningful diagnostic insights in two scenarios: a negative antibody titer strongly decreases the likelihood of FIP (high negative predictive value) and a serum high antibody titer (>1:1600) increases the probability of FIP (positive predictive value of 94 %).[7,15,18] The frequency of FCoV serology testing likely reflects the ease of blood sampling compared to organ sampling, and a limited understanding of its diagnostic value. This highlights the importance of emphasizing that FIP diagnosis should never rely solely on serology, especially in primary care settings.

Reports of SPE were available in 20 % of cats in this study. This test is useful to differentiate monoclonal from polyclonal gammopathy and aids in discriminating inflammatory/infectious processes from neoplastic processes.[3] In this study, it is not possible to determine if clinicians intended to rule out neoplastic processes or if they just performed this test following the advice of the Facebook group administrators. In the second case, serum electrophoresis offers no diagnostic advantage over routine blood proteins measurement, and its use should be discouraged to avoid unnecessary testing and additional costs.

Interestingly, hyporexia/anorexia was more commonly documented in cats with effusive FIP. One possibility is that the presence of effusion causes more discomfort. Alternatively, these cats might have been more severely ill, as effusive FIP is recognized to have a more acute onset, in contrast to non-effusive FIP, which typically follows a more chronic course.[14–16] At the same time, cats with effusive FIP more frequently showed hypoalbuminemia (P <0,001), which is mainly attributable to losses into effusions and, to a lesser extent, to a reduction related to its role as negative acute-phase protein.[11,13] In contrast, cats with non-effusive FIP had significantly more frequent hyperproteinemia (P <0,001) and showed less hypoalbuminemia. This might also reflect a more chronic immune response, allowing for sustained hyperglobulinemia without concurrent protein loss.[13,16] Since non-effusive FIP is more challenging to confirm than effusive FIP, the presence of hyperproteinemia might often be one decisive finding in establishing the suspicion of FIP.

Further analysis of deceased cats would have been necessary to assess potential differences in their diagnostic approach, causes of treatment failure, and possible misdiagnoses, which are particularly relevant in light of limited diagnostic testing. Unfortunately, information on this population was incomplete. Characterizing misdiagnosed cases would be useful to identify patterns and better guide practitioners. Although current guidelines recommend a therapeutic trial with GS-441524 if the suspicion of FIP is high, valuable time might be lost if the diagnosis is incorrect.[12] Conversely, refractory cases would raise major concerns about antiviral resistance. This phenomenon is well described in human medicine, where antiviral resistance is more likely to occur in immunocompromised patients undergoing long-

term single-agent antiviral therapy.[9,10] Following the SARS-CoV-2 pandemic, a study demonstrated very low rates of resistance to remdesivir despite its massive use over an 18-month period.[23] Little is known about antiviral resistance in small animals, and further investigations are needed.

This study has several limitations. The dataset was obtained retrospectively through a social media platform, which inherently carries variable quality of information, incomplete records, and dependence on non-medical personnel for documentation. These factors may have affected data reliability and accuracy and should be considered as a major limitation. Consequently, the results for the initial diagnostic approach may be underestimated, though not to a degree likely to invalidate the overall analysis. Additionally, the use of GS-441524 was not in accordance with the existing legal framework. The inclusion of data derived from such treatment protocols introduces important limitations including: the lack of regulatory oversight regarding drug quality and formulation, the absence of standardized treatment protocols, and potential variability in dosing, monitoring, and supportive care among practices. Another limitation concerns diagnostic certainty: only a minority of cases underwent confirmatory testing (PCR or immunohistochemistry), and none were confirmed by histopathology. Consequently, most cases were categorized as «highly suspicious» rather than definitively diagnosed, which may have introduced a risk of misclassification or misdiagnosis; however this is also in accordance to a previous study reporting the use of licensed GS-441524 to treat 307 cats.[17] The distribution of FIP forms may have been biased by the limited number of reported imaging studies. Likewise, the absence of systematic neurologic and ophthalmologic evaluations may have led to underreporting of neurologic or ocular involvement. Another limitation includes laboratory results variability: diagnostic testing was performed across various laboratories, including both in-house and external facilities, possibly using different analytical methods and reference intervals. As a result, some variability in test performance and interpretation is inevitable, and the results may not be directly comparable across cases. Finally, missing data on deceased cats limited the assessment of misdiagnoses or treatment failures, which may differ between primary care and referral settings. As all the deceased cats were excluded, this may also have introduced a selection bias. However, as the number of deceased cats was very small compared with the total number of cats, it was therefore deemed unlikely that their inclusion would have substantially altered the overall results.

## Conclusion

The study suggests that in primary care settings, a diagnosis of FIP is often based on signalment, clinical signs, and basic blood work. Clinical criteria should be defined to identify cases where confirmatory testing, such as RT-PCR for FCoV or cytology, is strongly recommended, to prevent misdiagnoses and the inappropriate use of antiviral treatments.

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## Traitement antiviral non autorisé avec le GS-441524: comment les cliniciens abordent-ils la péritonite infectieuse féline dans les cabinets de soins primaires?

La disponibilité mondiale du GS-441524 pour le traitement de la péritonite infectieuse féline (PIF) a augmenté ces dernières années, mais peu de données sont disponibles sur la manière dont les vétérinaires de soins primaires diagnostiquent la maladie. Cette étude visait à évaluer l'approche diagnostique de la PIF dans les cabinets de soins primaires et à comparer les résultats entre les formes effusive et non effusive.

Une analyse rétrospective a été réalisée à partir d'un ensemble de données concernant 243 chats traités en Suisse romande durant au moins 12 semaines avec du GS-441524 non autorisé, données obtenues via une plateforme de réseau social.

Les données démographiques étaient conformes aux rapports précédents. Les formes effusive et non effusive de la PIF étaient représentées de manière égale. Les symptômes les plus fréquents étaient l'hyporexie/anorexie (70 %; 166/236), la perte de poids (63 %; 149/236) et la léthargie (59 %; 140/236). L'hyporexie/anorexie était plus fréquente chez les chats atteints de PIF effusive (P < 0,001). Les tests diagnostiques les plus courants comprenaient la numération globulaire complète et la biochimie (92 %; 224/243 chacun), les titrages d'anticorps sériques anti-FCoV (28 %; 69/243), la PCR anti-FCoV (28 %; 69/243), l'amyloïde A sérique (SAA) (27 %; 65/243), l'électrophorèse des protéines sériques (20 %; 48/243) et l'échographie abdominale (19 %; 46/243). Les chats atteints de PIF effusive étaient plus susceptibles de subir un test PCR FCoV que les chats atteints de PIF non effusive (P < 0,001). À l'inverse, les chats atteints de PIF non effusive avaient plus souvent des titres FCoV disponibles (P < 0,001). Les anomalies biologiques les plus courantes comprenaient l'hyperglobulinémie (80 %; 179/223), l'augmentation du SAA (78 %; 51/65), l'anémie (55 %; 124/224), l'hyperprotéinémie (54 %; 123/227) et un rapport albumine/globuline < 0,4 (53 %; 120/225). L'hyperprotéinémie était significativement plus fréquente chez les chats atteints de PIF non effusive (67 %; 76/114; P < 0,001), tandis que l'hypoalbuminémie était significativement plus fréquente chez les chats atteints de PIF effusive (39 %; 43/111; P < 0,001).

Ces résultats démontrent que la décision de traiter les chats avec le GS-441524 en soins primaires repose sur un diagnostic présomptif avec un minimum de tests diagnostiques. Des critères doivent être définis pour identifier les cas où des tests de confirmation, tels que la RT-PCR pour le FCoV, sont essentiels, afin d'éviter les erreurs de diagnostic et l'utilisation inappropriée d'antiviraux.

**Mots clés:** chat, coronavirus, effusif, sec, FCoV, PIF.

## Trattamento antivirale non autorizzato con GS-441524: come i veterinari clinici affrontano la peritonite infettiva felina (FIP) nella pratica veterinaria di base?

La disponibilità globale di GS-441524 per il trattamento della peritonite infettiva felina (FIP) è aumentata negli ultimi anni, tuttavia sono disponibili pochi dati su come le pratiche veterinarie formulino la diagnosi. Questo studio aveva l'obiettivo di valutare l'approccio diagnostico alla FIP nelle pratiche veterinarie di medicina generale e confrontare i risultati tra le forme essudative e non essudative.

È stata condotta un'analisi retrospettiva utilizzando un dataset di 243 gatti trattati con il non autorizzato GS-441524 nella Svizzera occidentale, ottenuto tramite una piattaforma social, tutti sottoposti a un trattamento minimo di 12 settimane.

I dati demografici erano coerenti con quanto riportato in precedenza. Le forme essudativa e non essudativa di FIP erano rappresentate in ugual misura. I segni clinici più comuni includevano iporessia/anoressia (70 %; 166/236), perdita di peso (63 %; 149/236) e letargia (59 %; 140/236). L'iporessia/anoressia era più frequente nei gatti con FIP essudativa (P < 0,001). Gli esami diagnostici più comunemente eseguiti comprendevano emocromo completo e profilo biochimico (92 %; 224/243 ciascuno), titoli anticorpali anti-FCoV (28 %; 69/243), PCR per FCoV (28 %; 69/243), siero amiloide A (SAA) (27 %; 65/243), elettroforesi delle proteine sieriche (20 %; 48/243) ed ecografia addominale (19 %; 46/243). I gatti con FIP essudativa avevano maggiori probabilità di essere sottoposti a PCR per FCoV rispetto ai gatti con FIP non essudativa (P < 0,001). Al contrario, nei gatti con FIP non essudativa erano più frequentemente disponibili i risultati dei titoli anticorpali anti-FCoV (P < 0,001).

Le anomalie di laboratorio più comuni comprendevano iperglobulinemia (80 %; 179/223), aumento della SAA (78 %; 51/65), anemia (55 %; 124/224), iperproteinemia (54 %; 123/227) e un rapporto albumina/globuline < 0,4 (53 %; 120/225). L'iperproteinemia era significativamente più frequente nei gatti con FIP non essudativa (67 %; 76/114; P < 0,001), mentre l'ipoalbuminemia era significativamente più comune nei gatti con FIP essudativa (39 %; 43/111; P < 0,001). Questi risultati dimostrano che la decisione di trattare i gatti con GS-441524 nella medicina veterinaria di base si appoggia spesso su una diagnosi presuntiva con un numero minimo di test diagnostici. È necessario definire criteri chiari per identificare i casi in cui sono essenziali test confermativi, come la RT-PCR per FCoV, al fine di prevenire diagnosi errate e un uso inappropriato degli antivirali.

**Parole chiave:** gatto, coronavirus, essudativa, secca, FCoV, FIP.

Unlicensed antiviral treatment with GS-441524: How are clinicians approaching feline infectious peritonitis in primary care practices?

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## Korrespondenzadresse

Alexandra Schlachet
Kleintierklinik Universität Bern
Länggastrassse 128
CH-3012 Bern
E-Mail: alexandra.schlachet@unibe.ch