Journal of Feline Medicine and Surgery (2010) **12**, 262–268
doi:10.1016/j.jfms.2009.09.007

ELSEVIER

jfms

Evaluation of adverse events in cats receiving long-term piroxicam therapy for various neoplasms

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The role of cyclo-oxygenase 2 (COX-2) and prostaglandins (PG) in carcinogenesis has been documented in many species. Piroxicam has shown efficacy against several neoplasms and is frequently prescribed for chronic use. There are no studies investigating chronic piroxicam administration in cats and the chronic use of non-steroidal anti-inflammatory agents in this species has long been cautioned against. This retrospective study aimed to evaluate adverse effects in cats receiving long-term daily piroxicam. Seventy-three cats received daily piroxicam at doses of 0.13–0.41 mg/kg. Treatment duration ranged from 1 to 38 months. Treatment with piroxicam was found to significantly increase frequency of vomiting during the first month of therapy, though this was most significant for cats receiving concurrent chemotherapy. Piroxicam administration was not significantly associated with hematologic, renal or hepatic toxicities. Adverse events were not correlated with dosage. Adverse events were reported in 29% of cats, and were generally mild and transient. Eight percent discontinued piroxicam due to adverse reaction, and 4% due to difficult administration. This study indicates that long-term daily piroxicam is generally well tolerated in cats at conventional doses.

Date accepted: 7 September 2009

The role of cyclo-oxygenase (COX) enzymes and prostaglandins (PG) in tumor growth and promotion has been well documented in many human, rodent, canine and feline tumors. COX-2 can be induced by many disorders, including several oncogenes.[1–3] COX-2 over-expression has been documented in feline squamous cell and transitional cell carcinomas,[4–6] and piroxicam is often used for other tumors based on canine and human studies.[7–9] The precise mechanism of the anti-tumor activity of piroxicam is unknown.[10] In general, use of non-steroidal anti-inflammatory drugs (NSAIDs) has been approached with caution in cats due to the extensive hepatic metabolism required in most species and the limited glucuronidation capacity of feline hepatocytes.[3,10–12] Only one NSAID, meloxicam (Metacam; Bohringer AH) is currently labeled for use in cats in the United States, though oral tolfenamic acid (Tolfedine; Vetoquinol), carprofen (single use, Rimadyl; Pfizer) and meloxicam are licensed in Canada (short-term use) and Europe (short- and long-term use). No NSAID is currently approved for chronic use in the cat.

Single and multi-dose pharmacokinetics of piroxicam has been established in the cat. Heeb et al[10,12] found that 0.3 mg/kg appeared well tolerated as a single oral or intravenous dose, and also when dosed orally for 10 consecutive days. There is very little published information on the clinical use of piroxicam in cats and the effective dose is unknown. One report evaluating treatment options for cats with transitional cell carcinoma included seven cats which received oral piroxicam at 0.3 mg/kg every 3–4 days.[13] Response was variable, and melena and anemia were reported in one cat. Intracavitary carboplatin and oral piroxicam were administered to a cat with malignant mesothelioma.[14] This cat also experienced melena and anemia but continued piroxicam after a 1 week hiatus and survived 6 months after diagnosis.

The primary objective of this study was to evaluate the clinical safety of long-term piroxicam use in cats, and to determine the most common adverse effects. A secondary objective was to determine whether piroxicam in combination with other cancer treatment modalities showed additive toxicity and to determine whether this toxicity was acceptable. This study will

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1098-612X/09/040262+07 $36.00/0

facilitate future investigations into the efficacy of piroxicam as an anti-neoplastic therapy for cats.

Materials and methods

A retrospective search was conducted through the Veterinary Cancer Group database for feline patients prescribed 1 mg capsules of compounded piroxicam from July 2006 to July 2008. The resulting medical records were reviewed to find suitable subjects. Cases were included if the patient had a complete blood count, serum biochemical profile (including a minimum of serum albumin, alkaline phosphatase, alanine aminotransferase (ALT), blood urea nitrogen, creatinine, glucose and total protein) and urinalysis prior to being prescribed piroxicam, had received oral piroxicam daily for a minimum of 14 days and had at least one evaluation including laboratory analysis (minimum complete blood count and serum creatinine) after receiving piroxicam for at least 14 days. Cats receiving piroxicam for gastrointestinal neoplasia were excluded from the study.

Data collected from the medical records included signalment; presenting complaint; tumor type; concurrent diseases; hematology, serum biochemistry and urinalysis results; concurrent treatments including chemotherapy; and incidence and severity of adverse events. Records were assessed for hematological and biochemical changes, as well as for side effects reported by the owner(s) while the cat was receiving piroxicam. Toxicity was determined by evaluating changes in laboratory parameters, physical examination and spontaneous reporting of adverse effects at home. Evaluations were conducted on a case-by-case basis as dictated by concurrent treatment schedule or at the clinicians' discretion. The duration of therapy and reason for discontinuation was determined, as was the last known status and cause of death if available. Patients lost to follow-up were included in the study so long as they fulfilled the initial criteria, and were censored at the date of last contact.

The incidence of adverse effects during and beyond the first month of therapy was compared to the incidence prior to beginning therapy based on clinician and owner reports and laboratory analysis. Where the frequency of adverse effects was significantly different before and after beginning piroxicam, results were also analyzed for differences between cats receiving piroxicam alone (group A); piroxicam and radiation therapy (group B); piroxicam and chemotherapy (group C); or piroxicam, radiation and chemotherapy (group D). Significance of results was determined using McNemar's χ^2-test with Yates continuity correction for dependent variables, Pearson's χ^2 analysis with Yates continuity correction for independent variables and Kruskal–Wallis χ^2 analysis for continuous variables. Significance was set at $P < 0.05$. When a small sample size was affected, a simulation-based test was also performed to support the statistical findings. Where applicable, relative risk was also assessed. The number of cats with hematologic changes, or elevations of renal or hepatic parameters within a set time period was compared to the number of cats having these values assessed during that time period to also evaluate for trends which did not reach statistical significance.

Results

Seventy-three cats fulfilled the study criteria. Forty-six cats were castrated males, and 27 were spayed females. The age range was 6–18 years, with a mean age of 12.8 years. Domestic shorthair cats comprised the majority of cats (74%), though many breeds were represented. Squamous cell carcinoma was the most frequent diagnosis (51%), followed by nasal adenocarcinoma (15%). Mammary gland adenocarcinoma, transitional cell carcinoma, hemangiosarcoma, amelanotic melanoma, fibrosarcoma, pulmonary carcinoma, soft tissue sarcoma, osteochondrosarcoma, anal gland sebaceous adenocarcinoma, plasmacytoma, and vulvar adenocarcinoma were also treated with piroxicam. Metastases were documented in 11 cats (15%).

Hyperthyroidism was the most common concurrent disease (3%). One cat had been previously diagnosed with chronic renal insufficiency which was stable prior to beginning therapy. Two other cats had histories of lower urinary tract disease and crystalluria.

Piroxicam was the sole therapy in 28 cats (38%). Piroxicam was also frequently prescribed as multimodal therapy. Piroxicam was administered to 20 cats receiving concurrent radiation therapy; 12 of these 20 cats received piroxicam, radiation and chemotherapy. Three cats underwent surgery to address their primary disease and received piroxicam as adjunct therapy. Piroxicam was also administered to 25 cats receiving various chemotherapeutic agents, including doxorubicin (11 cats), cyclophosphamide (five cats), carboplatin (29 cats), gemcitabine (10 cats), mitoxantrone (five cats), and combinations of these chemotherapeutics. Other common concurrent medications included methimazole, amoxicillin–clavulanic acid and enrofloxacin. Two cats were administered misoprostol concurrently (4 μg/kg PO q 12 h). Piroxicam was most frequently administered at 1 mg/cat orally once a day (97%), though two large cats (7.8 and 8.1 kg) received 2 mg/cat, orally, once daily. This resulted in a wide range of doses being administered (0.13–0.41 mg/kg; mean 0.22 mg/kg, median 0.235 mg/kg, mode 0.29 mg/kg).

Pre-treatment complete blood counts were within normal limits in 71/73 cases. Two cats showed a mild mature neutrophilia (segmented neutrophil counts 14.5 and 15.2×10^9/l). Azotemia (serum creatinine above 2.3 mg/dl; reference range 0.8–2.3 mg/dl) was noted in 10 cats prior to beginning piroxicam, and determined to be pre-renal (urine specific gravity [USG] above 1.035) in six cats. Of the remaining four

cats, one was known to have stable renal insufficiency prior to referral. Hyperglobulinemia (serum globulins 8.7 g/dl; reference range 3–5.6 g/dl) was noted in one cat with oral squamous cell carcinoma. An elevation in serum ALT was noted in one cat (147 U/l; reference range 28–100 U/l) which also had renal azotemia. Hematuria was noted on two cats with bladder transitional cell carcinoma.

No significant differences were noted in signalment, concurrent disease or frequency of adverse events between the treatment groups prior to starting treatment. There was no significant difference in median piroxicam dosage between treatment groups (Krusal–Wallis $\chi^2 = 1.916$, $P = 0.59$). Cats in group A received a median of 0.24 mg/kg (range 0.13–0.41 mg/kg); group B a median of 0.24 mg/kg (range 0.17–0.29 mg/kg); group C a median of 0.25 mg/kg (range 0.13–0.40 mg/kg) and group D a median of 0.24 mg/kg (range 0.17–0.30 mg/kg).

During the first month of piroxicam therapy, vomiting was reported in 12/73 cats (16.4%). Vomiting was significantly correlated with piroxicam administration when compared to pre-treatment (McNemars' $\chi^2 = 10.08$; $P = 0.0015$, simulation-based test with 2000 replications $P = 0.0010$; Table 1). Most owners reported once weekly or intermittent vomiting during this period. When cats were divided into treatment groups, vomiting was found to be significantly more frequent in cats receiving chemotherapy and piroxicam (groups C and D) than when compared to those receiving piroxicam alone or piroxicam with radiation therapy (groups A and B) (Table 2; Pearson's $\chi^2 = 4.66$; $P = 0.0309$). Cats receiving piroxicam and concurrent chemotherapy were 4.8 times more likely to experience vomiting than cats receiving piroxicam and no chemotherapeutic agents. Vomiting was reported most often for cats receiving doxorubicin or carboplatin.

A complete blood count and serum biochemical profile taken within the first month of therapy after beginning piroxicam was available for 43/73 cats. Neutropenia was noted in four cats receiving piroxicam with concurrent chemotherapy; but this occurrence was neither clinically nor statistically significant. No significant changes in renal or hepatic parameters were found. The four cats with evidence of renal insufficiency prior to starting piroxicam had unchanged renal values. Median pre-treatment serum creatinine was 1.8 mg/dl (range 0.8–3.1 mg/dl). Median serum creatinine when assessed during the first month of treatment was 1.7 mg/dl (range 0.8–3.1 mg/dl). Median serum ALT was 47 U/l (range 16–149 U/l) prior to treatment, and 48 U/l (range 22–89 U/l) when assessed within the first month of therapy. No hematologic abnormalities were noted.

Within the first 3–6 weeks after presentation, four cats were euthanased due to progression of local disease and one due to metastases. Eight cats were lost to follow-up after their first re-evaluation. Three owners chose to discontinue piroxicam due to difficult administration.

Data was available beyond the initial month for 82% of cases although 28 patients were ultimately lost to follow-up. The majority of patients who continued piroxicam after the initial month continued to receive daily piroxicam until the time of euthanasia or natural death. The range of treatment time was 4 weeks to 38 months (median 4.5 months, mean 5.2 months). Piroxicam therapy was stopped in two cats after 8 and 11 weeks of treatment due to increased frequency of vomiting, however, the total incidence of vomiting was not significantly increased when compared to pre-treatment (Table 1). Table 3 illustrates the number of cats remaining on study at subsequent time periods, as well as analysis of renal and hepatic parameters during these times. Complete blood counts and biochemical profiles were performed at the clinicians' discretion or as indicated by concurrent treatments.

One patient with initially normal renal parameters developed azotemia (creatinine 2.5 mg/dl; USG not reported) after receiving piroxicam (0.19 mg/kg PO q 24 h) for 5 weeks and subsequently discontinued administration. Piroxicam (0.24 mg/kg PO q 24 h) was also discontinued in one cat after 8 months of therapy due to azotemia (creatinine 2.4 mg/dl, USG not reported). A third cat for which serum creatinine

Table 1. Frequency of adverse events before starting piroxicam, during and beyond the first month of treatment with piroxicam (range 1–38 months).

	Number of cats on study	Vomiting	Diarrhea	Decreased appetite	Altered CBC	Renal disease	Elevated liver enzymes
Prior to therapy	73	0	0	0	0	4 (5.5%)	1 (1.3%)
During first month	73	12* (16.4%)	2 (2.7%)	2 (2.7%)	4 (5.5%)	4 (5.5%)	0
Overall beyond first month therapy	58	2 (3.4%)	0	1 (1.7%)	0	5 (8.6%)	2 (3.4%)

CBC = complete blood count.
*Denotes statistically significant difference from prior incidence ($P < 0.05$).

Table 2. Frequency of vomiting (percent of cats) during the first month of piroxicam therapy with cats separated into treatment groups.

	Group A: piroxicam	Group B: piroxicam and radiation	Group C: piroxicam and chemotherapy	Group D: piroxicam, chemotherapy and radiation
Number of cats	28	8	25	12
Incidence of vomiting prior to therapy	0	0	0	0
Incidence of vomiting during first month	1 (3.6%)	0	7* (28.0%)	3* (25.0%)

*Denotes statistically significant difference from prior frequency within the same treatment group ($P < 0.05$).

measurements were available every 3 months and were within the normal range until 35 months after starting piroxicam developed renal azotemia at 35 months (serum creatinine 4.7 mg/dl, USG 1.020) and therapy was then discontinued. Azotemia (serum creatinine 3.5 mg/dl, USG 1.022) was also noted in one cat after receiving 0.20 mg/kg piroxicam daily for 4 months, and piroxicam treatment was reduced to 0.20 mg/kg every 48 h. The cat survived a further 2 months with stable azotemia and no clinical signs associated with renal disease. A second cat had a similar reduction after developing mild azotemia (serum creatinine 2.3 mg/dl; USG not reported) after 8.5 months of 0.16 mg/kg piroxicam daily. Overall, five new cases of suspected renal insufficiency were detected in 58 cats receiving piroxicam for greater than 1 month in the present study. Median serum creatinine concentration did not differ from prior to therapy when cats were assessed at 1−3 months (1.6 mg/dl, range 0.9−2.5 mg/dl); 3−6 months (1.6 mg/dl, range 1.1−2.4 mg/dl); 6−12 months (1.8 mg/dl, range 0.8−3.5 mg/dl) and 12−24 months (1.9 mg/dl, range 0.8−3.1 mg/dl). The two cats remaining on study greater than 2 years had serum creatinine concentrations of 4.7 mg/dl (USG 1.020) and 1.3 mg/dl during this time frame.

Assessment of serum ALT concentration was available in 37 cats beyond the first month of therapy. Elevated ALT was an incidental finding in two cats, one after 4 months of piroxicam therapy (ALT 146 U/l, reference range 28−100 U/l) and the other 9 months after beginning piroxicam (ALT 172 U/l). Subsequent

Table 3. Distribution of hematologic, renal and hepatic evaluations over time and the incidence of associated toxicity for cats remaining on study during the indicated time period. Not all cats were evaluated for each interval. Please see text for details.

	Number of cats on study	Number of cats having serum creatinine evaluation in this period	Number of cats having USG in this period	Number of cats with renal disease	Number of cats having serum liver enzyme evaluation during this period	Number of cats with elevated liver enzymes	Number of cats having a CBC during this time period	Number of cats with anemia
Prior to therapy	73	73	19	4	65	1	73	0
During first month	73	43	2	4	19	0	45	0
Months 1−3	58	25	2	1	13	13	31	0
Months 3−6	46	23	6	1	19	1	27	1
Months 6−12	25	15	3	1	13	1	16	0
Months 12−24	10	8	3	2	8	0	6	0
Months 24+	2	2	0	1	1	0	2	0

CBC = complete blood count.

biochemical profiles taken at 6 and 10 months, respectively, were available for both cats, and showed normal serum ALT. Median ALT concentration was 49 U/l (range 30–90 U/l) when assessed between 1 and 3 months; 56 U/l (range 31–146 U/l) between 3 and 6 months; 46 U/l (range 18–172 U/l) at 6–12 months, and 55 U/l (range 38–86 U/l) from 12 to 24 months. Only one cat had serum ALT measurement beyond this point (36 U/l).

No hematologic abnormalities were recorded for cats treated beyond 1 month. Neutropenia was noted in several cats receiving concurrent chemotherapy within the first month of chemotherapy; however, these changes did not persist. In particular, anemia was not noted. Pre-treatment median hematocrit was 0.37 l/l (range 0.29–0.45 l/l). Median hematocrit did not differ when cats were assessed within 3 (median 0.35 l/l, range 0.29–0.45 l/l), 6 (median 0.35 l/l, range 0.30–0.39 l/l), 12 (median 0.35 l/l, range 0.29–0.43 l/l) or 24 months (median 0.37 l/l, range 0.32–0.41 l/l).

Overall, 21/73 cats (29%) experienced an adverse event during the first month of piroxicam therapy. Fifteen percent (9/58 cats) had adverse effects when evaluated beyond 1 month.

For the 45 cats with known status, progressive disease was the cause of death in 29 cats. Four cats succumbed to metastatic disease. One cat died of heart failure. Cause of death was unknown or unavailable in four cases. Seven patients were alive at the time of writing.

Discussion

In the population of cats in this study, most cats tolerated daily oral piroxicam beyond 1 month with no adverse effects. The most common adverse effect during the first month of therapy was vomiting. Vomiting was 4.8 times more likely in cats receiving concurrent chemotherapy than in cats receiving piroxicam alone. Given the retrospective nature of this study, it is difficult to evaluate the relative contribution of piroxicam and chemotherapy, however, vomiting was generally mild and did not require symptomatic therapy or cessation of either piroxicam or chemotherapy treatment. A case-control study with case-matched cats receiving chemotherapy with and without adjunct piroxicam would be necessary to truly evaluate these effects. Vomiting was not a dose or treatment limiting event. No acute hepatic, hematologic or hepatic toxicity was noted.

When treated longer than 1 month, five cats experienced elevations in renal parameters, though none showed clinical signs of renal insufficiency according to their medical records. Determining the implication of this information is difficult as it would require knowledge of the incidence of renal disease within this cat population during this time if they were not treated with piroxicam. This may represent the incidence of renal toxicity for cats receiving long-term piroxicam. The population of cats in the current study could also be predisposed to developing renal disease either from age, effects of their cancer or from nephrotoxic effects of chemotherapy. Two of these cats received carboplatin; one cat received one treatment and the second received seven treatments in conjunction with gemcitabine. One cat received two treatments of doxorubicin prior to becoming azotemic. Carboplatin has not been shown to cause renal damage, while doxorubicin-related nephrotoxicity has been documented in cats.[15,16] Three of these cases occurred months (8, 8.5 and 35 months) after starting piroxicam, and so the role of piroxicam is unclear. Adverse events associated with NSAID use in dogs occurred most commonly between 14 and 30 days after beginning treatment (range 3–90 days) which does not fit with the occurrence of renal disease in this study.[17] The incidence of adverse events in cats is unknown, and may not follow the pattern seen in dogs. A case-control study would be needed to determine whether cats receiving piroxicam are at increased risk for renal disease than the general aging cat population. The occurrence of azotemia many months after initiating therapy emphasizes the need for monitoring of renal values for cats receiving piroxicam. Cats with renal azotemia prior to starting piroxicam did not appear to have progressive azotemia while receiving piroxicam.

NSAIDs are the largest group of drugs associated with adverse reactions.[3,17] In dogs, the most common adverse effects are associated with the gastrointestinal (64%), renal (21%) and hepatic (14%) systems.[3] NSAIDs impair renal autoregulation when hypovolemic or hypotensive; acute renal failure has been reported in cats and dogs following NSAID use.[3] The four most common adverse effects of NSAID toxicosis were vomiting, anorexia, depression and diarrhea.[2] NSAID administration is a known risk factor for gastrointestinal ulceration in cats, as COX inhibition has been shown as an important mechanism for deep gastrointestinal ulcers, and local PG production in cats regulates bicarbonate transport in the duodenum and stomach.[3] There are no reports of NSAID induced hepatotoxicity in cats.[3] The true incidence of adverse events in veterinary medicine is unknown.

Cats appear to be sensitive to the adverse effects of anti-inflammatory agents.[11] Most NSAIDs undergo hepatic metabolism through glucuronidation[3] and the limited ability for hepatic glucuronidation in cats is well established. Piroxicam forms a glucuronide conjugate during metabolism in people and in dogs.[10] Due to decreased metabolism, many NSAIDs have a longer half-life in cats than in dogs; however, piroxicam and meloxicam have a shorter half-life in cats. The half-life for piroxicam in cats is 12–13 h compared to 40 h in dogs.[3,10] These agents may be cleared by oxidative enzymes in cats, which may decrease the potential for toxicity.

Heeb et al[10] treated eight cats with a single dose of piroxicam (0.3 mg/kg) orally and intravenously to

determine single dose pharmacokinetics. All cats remained clinically healthy throughout the study, and no elevations in renal or hepatic parameters were noted. The mean maximum plasma concentration achieved in cats was 519 ng/ml, which is approximately half that achieved in dogs (1.35 μg/ml). The effective dose has not been determined, and adverse effects may rise if the dose was increased to achieve the concentration equivalent to that of dogs. Heeb et al[12] also evaluated multiple dose pharmacokinetics in cats. All cats were clinically healthy throughout the study, with no biochemical alterations noted. Cats received oral piroxicam (0.3 mg/kg) were evaluated endoscopically at days 0, 5 and 10, and 4/7 cats receiving piroxicam alone developed mild to severe gastric erosions but remained asymptomatic. Two of seven cats receiving piroxicam with cimetidine developed mild erosions.[12] Gastrointestinal erosions could have been missed in this study as it was dependent on clinical signs and was retrospective in nature.

In a retrospective study of 20 cats treated for transitional cell carcinoma, seven received oral piroxicam (0.3 mg/kg PO q 72−96 h).[13] One cat developed melena and anemia which resolved with the addition of misoprostol. One cat treated with concurrent doxorubicin and cyclophosphamide experienced neutropenia and vomiting. Spugnini et al[14] treated one cat with malignant mesothelioma with intracavitary carboplatin and subcutaneous piroxicam injections (0.3 mg/kg q 48 h) for 4 months. One episode of hematochezia was reported. The contribution of piroxicam to this adverse reaction is difficult to determine, as subcutaneous absorption has not been evaluated. Marioni-Henry et al[18] published a case report of a single cat with nasal adenocarcinoma invading the frontal lobe which was treated with piroxicam (0.3 mg/kg PO q 48 for 10 days then q 24) and misoprostol (4.7 μg/kg PO q 8 h) for 22 months without adverse event. The cat also received surgery and chemoembolization. Unpublished data cited in a review article by Lascelles et al[3] indicated that daily oral piroxicam can significantly decrease hematocrit in 30% of cats treated beyond 7−14 days. These findings were not supported in this study as the hematocrit remained stable in all cats. Hematochezia and melena were also not reported. It is possible that cats remained asymptomatic despite gastric erosions, as seen in the study by Heeb et al.[12] It is also possible that accurate information was not obtained from owners, and that subtle signs of gastrointestinal irritation were not detected by owners. It is also possible that a higher degree of toxicity was accepted by the owners given the nature of their pets' disease, and hence not reported. Clinical signs of renal toxicity were not noted in previously reported cases, nor identified in the present study. However, the occurrence of azotemia in several cats within the time frame of this study does raise concern. Given that mean plasma concentration in cats was approximately half that achieved in dogs receiving the same oral dose (0.3 mg/kg) of piroxicam, it could be that the standard dose of 0.3 mg/kg daily is too low to show efficacy or toxicity. Efficacy studies using this dose, or dose escalation studies would be needed to assess this possibility.

This study has inherent weaknesses due to its retrospective nature. The cats in this study were a diverse population, and were receiving a variety of concurrent treatments for different neoplasms. Monitoring and available follow-up information also varied between cats. While a large number of cats had periodic complete blood count and chemistry profiles performed, USG measurements were performed infrequently. This may have lead to over-diagnosis of renal disease if some cats truly had pre-renal azotemia. In this study, the occurrence of azotemia in the absence of a known USG measurement above 1.035 was interpreted as renal insufficiency so as to not underestimate toxicity. Conversely, loss of urine concentration ability occurs prior to the occurrence of azotemia, and so early cases of renal disease may have been undetected. However, this study is the first to evaluate the clinical use and long-term toxicity profile of piroxicam in cats, and the first to assess its use it combination with other cancer treatment modalities. Given the lack of COX-2 selectivity of piroxicam in most species, and the historic concern with NSAID toxicity in cats, adverse events were expected in this study. The cats in this study were frequently geriatric or compromised by their primary disease. Many cats were also receiving chemotherapy or were anesthetized for radiation therapy, both of which could potentiate the adverse effects of NSAIDs. Despite these factors, piroxicam appeared well tolerated. Only 8% of cats (6/73) stopped therapy due to adverse events. As piroxicam is now almost exclusively used in oncology, these cats are likely more representative of the target population than otherwise healthy cats.

This study found low toxicity with chronic use of piroxicam in cats. The clinical indications and efficacy in this species remain unknown. Future studies evaluating the clinical efficacy, effective dose and antineoplastic mechanisms of piroxicam are needed before the role of piroxicam in veterinary medicine can be fully determined. Additional studies investigating chronic use of other NSAIDs are also warranted.

Acknowledgements

The authors would like to thank Drs Autumn Dutelle, Sara Fiocchi and Jarrod Vancil for their advice and support, and also the staff of the Veterinary Cancer Group for their assistance.

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