Lomustine for treatment of mast cell tumors in cats: 38 cases (1999–2005)

Kenneth M. Rassnick, DVM, DACVIM; Laurel E. Williams, DVM, DACVIM;
Orna Kristal, DVM, DACVIM; Renée Al-Sarraf, DVM, DACVIM; Jennifer L. Baez, VMD, DACVIM;
Courtney H. Zwahlen, DVM, DACVIM; Gillian Dank, DVM, DACVIM

Objective—To determine clinical activity and toxic effects of lomustine when used to treat cats with mast cell tumors (MCTs).

Design—Retrospective case series.

Animals—38 cats with measurable, histologically or cytologically confirmed MCTs treated with lomustine at a dosage ≥ 50 mg/m^2.

Procedures—Medical records were reviewed to determine response to treatment and evidence of drug toxicoses. The Kaplan-Meier method was used to estimate remission duration.

Results—26 cats had cutaneous MCTs, 7 had MCTs of the mesenteric lymph nodes, 2 had gastrointestinal tract MCTs, 2 had hepatic MCTs, and 1 had MCTs involving multiple organs. Targeted lomustine dosage was 50 mg/m^2 in 22 cats and 60 mg/m^2 in 16 cats. Median administered dosage of lomustine was 56 mg/m^2 (range, 48 to 65 mg/m^2), and median number of doses administered was 2 (range, 1 to 12). Seven cats had a complete response and 12 had a partial response, for an overall response rate of 50%. Median response duration was 168 days (range, 25 to 727 days). The most common toxicoses were neutropenia and thrombocytopenia.

Conclusions and Clinical Relevance—Results suggested that lomustine had activity against MCTs in cats and was well tolerated. Further, findings suggested that treatment with lomustine should be considered for cats with MCTs for which local treatment is not an option. (*J Am Vet Med Assoc* 2008;232:1200–1205)

Mast cell tumors are common tumors of the skin, intestinal tract, and spleen in cats.[1] The biological behavior of MCTs in cats ranges from benign to malignant. Most cutaneous MCTs are benign, and recurrence or metastasis after excision or irradiation with radioactive strontium is rare.[2–7] In contrast, most MCTs of the intestinal tract in cats are associated with a poor prognosis because of their infiltrative nature, tendency to cause adhesions, and high likelihood for regional and distant metastasis.[8–12] Widespread dissemination and metastasis to the liver, visceral lymph nodes, bone marrow, and lung are common in cats with splenic MCTs.[1] However, even in those cats with other evidence of systemic involvement, splenectomy in cats with splenic MCTs has been associated with long survival times, with 1 study[13] reporting a median survival time of 19 months.

Surgery or radiation therapy is the most common treatment for cats with MCTs. Alternative systemic treatments, however, are needed for those cats in which surgery or radiation therapy is not possible or has not been successful (eg, cats with cutaneous or intestinal MCTs that are not resectable or are metastatic or recurrent). In addition, adjuvant systemic treatment might help improve tumor control and survival time following surgery in certain cats with MCTs, such as cats with intestinal MCTs that have undergone resection and cats with splenic MCTs that do not improve or have a recurrence after splenectomy. To our knowledge, however, there have been no published studies evaluating response to various systemic treatments in cats with MCTs.

Abbreviations

MCT	Mast cell tumor
CI	Confidence interval

From the Department of Clinical Sciences, College of Veterinary Medicine, Cornell University, Ithaca, NY 14853 (Rassnick); the Department of Clinical Sciences, College of Veterinary Medicine, North Carolina State University, Raleigh, NC 27606 (Williams); Animal Cancer Specialists, 11536 Lake City Way NE, Seattle, WA 98125 (Kristal); Animal Emergency and Referral Associates, 1237 Bloomfield Ave, Fairfield, NJ 07004 (Al-Sarraf); the Department of Clinical Sciences, School of Veterinary Medicine, University of Pennsylvania, Philadelphia, PA 19104 (Baez); Veterinary Cancer Referral Group, 2965 Edinger Ave, Tustin, CA 92780 (Zwahlen); and Koret School of Veterinary Medicine, The Hebrew University of Jerusalem, POB 12, Rehovot 76100, Israel (Dank). Dr. Kristal's present address is Chavat Daat Veterinary Specialty Center, Bet Berl, Kfar Saba, 44905, Israel. Dr. Baez's present address is Center for Animal Referral and Emergency Services, 2010 Cabot Blvd, Langhorne, PA 19047. Dr. Zwahlen's present address is Southern California Veterinary Referral Group, 1371 Reynolds Ave, Irvine, CA 92614.

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Address correspondence to Dr. Rassnick.

In dogs with measurable MCTs, lomustine is an effective systemic treatment, with an overall response rate of 42%.[14] Acute neutropenia and hepatic damage are the principal toxic effects of lomustine in dogs.[14–16] Other adverse effects documented uncommonly in dogs treated with lomustine include delayed and cumulative effects on the bone marrow,[15] renal toxicosis,[16] bicavitary effusion,[16] and unexplained fever.[15] In a phase I study to determine the maximum tolerated dose of lomustine and dose-limiting toxicoses associated with a single dose of lomustine in cats with various tumors, 1 cat with multiple cutaneous MCTs had a > 50% reduction in tumor burden.[17] Neutropenia was concluded to be the acute dose-limiting adverse effect of lomustine in cats, and a dosage of 50 to 60 mg/m^2 was recommended for future phase II trials.[17] In another study,[18] 3 cats with visceral MCTs were treated with lomustine but response could not be determined because only microscopic disease was present. A low incidence of myelosuppression was reported in that study,[18] but because cats received a standard dose of lomustine (10 mg) regardless of body weight, the dosage of lomustine was < 50 mg/m^2 in at least half of the 20 cats studied.

Taken together, these previous findings suggest that lomustine may be an effective systemic treatment for MCTs in cats. The purpose of the study reported here was to determine clinical activity and toxic effects of lomustine when used to treat cats with measurable MCTs.

Materials and Methods

Case selection criteria—Medical records of 15 institutions were searched to identify cats with MCTs treated with lomustine[a] between May 1999 and January 2005. Cats were eligible for inclusion in the study if the diagnosis of MCT had been confirmed histologically or cytologically, the cat had 1 or more measurable tumors, the targeted lomustine dosage was ≥ 50 mg/m^2 of body surface area, and no concurrent treatments (including corticosteroids and antihistamines) for the MCTs had been administered. Cats without measurable tumors, cats treated with lomustine as an adjunct to other treatments, and cats treated with lomustine at a targeted dosage < 50 mg/m^2 were excluded.

Medical records review—Information obtained from the medical records of cats included in the study consisted of signalment (breed, age, sex, and body weight), initial clinical signs, results of staging tests, method used to confirm the diagnosis of MCT, anatomic sites affected, and response to any previous treatment such as chemotherapy or surgery. In addition, information regarding each lomustine treatment was recorded, including date of administration, body weight at the time of administration, prescribed dosage, and administered dose. For purposes of the present study, cutaneous MCTs were classified as primary if the cat did not have any history of splenic MCT and as secondary if the cat had a history of splenic MCT.

Assessment of response—Response to treatment as assessed by the attending clinician was recorded for each treatment and categorized as a complete response (ie, disappearance of all clinical evidence of disease for at least 21 days), partial response (ie, ≥ 50% reduction but < 100% reduction in size of all measurable tumors for at least 21 days), or no response (ie, < 50% reduction in size of measurable tumors, increase in size of measurable tumors, appearance of new neoplastic lesions, or a complete or partial response persisting for < 21 days). The specific method (eg, caliper measurement or measurement on radiographic or ultrasonographic images) used to assess response depended on the anatomic site affected. The assessment schedule was generally defined as a multiple of the lomustine treatment cycle; however, treatment cycle length varied among cats. Cats that died, regardless of cause, or were lost to follow-up before 21 days were considered to have not responded.

Assessment of toxicoses—Evidence of lomustine-associated toxic effects was evaluated by examination of neutrophil counts, platelet counts, and results of serum biochemical analyses. Medical histories obtained from cat owners were used to assess gastrointestinal tract toxicoses. All toxic effects were graded in accordance with standard criteria.[19]

Statistical analysis—All cats that began treatment with lomustine were included in analyses of response rate and duration. Standard methods were used to calculate 95% CIs for response rate and response duration. Overall response rate was defined as the number of cats with a complete or partial response divided by the number of cats treated. Complete and partial response rates were defined as numbers of cats with a complete or partial response divided by the number of cats treated. Response duration was calculated by use of the Kaplan-Meier method. Because information on the exact date on which a response was achieved was not available for all cats, response duration was defined as the time from the first day of lomustine treatment until relapse for cats with a complete response, progression of disease for cats with a partial response, or death associated with lomustine toxicosis. Cats still in remission, cats lost to follow-up, and cats that died of some intercurrent disease were included in analyses until the last day follow-up information was collected and then were censored. Hematologic toxic effects were summarized by means of summary statistics, and hematologic nadirs were reported as a minimum value for each cat and each treatment. Nonhematologic toxic effects were summarized as maximum grade for each specific type of event for each treatment.

Results

Cats—Sixty-eight cats with MCTs treated with lomustine were initially identified during the retrospective search of medical records. Of these, 38 met the criteria for inclusion in the study, and 30 were excluded because targeted lomustine dosage was < 50 mg/m^2 (n = 22) or lomustine was administered as an adjunct in cats without measurable tumors (8).

Median age of the 38 cats included in the study was 11 years (range, 5 to 17 years). There were 20 spayed females and 18 castrated males. Most cats were domestic shorthairs (n = 23) or domestic longhairs (12). In

addition, there were 2 Maine Coon cats and 1 Somali. Cats weighed between 2.8 and 8.4 kg (6.2 and 18.5 lb; median, 4.4 kg [9.7 lb]).

Twenty-six of the 38 (68%) cats had cutaneous MCTs (20 with primary cutaneous MCTs and 6 with secondary cutaneous MCTs); 7 (18%) had MCTs of the mesenteric lymph nodes; 2 (5%) had gastrointestinal tract MCTs; 2 (5%) had hepatic MCTs; and 1 (3%) had MCTs involving the spleen, nasal cavity, and ipsilateral mandibular lymph node. In 13 of the 26 cats with cutaneous MCTs, lesions were too numerous to count. The remaining 13 cats had between 1 and 20 lesions (median, 3). Staging tests did not indicate any other primary location in the 7 cats with MCTs of the mesenteric lymph nodes, but splenic and hepatic aspirates were obtained in only 1 of these cats. The diagnosis of MCT was obtained histologically in 30 (79%) cats and cytologically in 8 (21%). Of the 8 cats in which the diagnosis was confirmed cytologically, 5 had multiple cutaneous MCTs; 2 had MCTs of mesenteric lymph nodes; and 1 had MCTs involving the spleen, nasal cavity, and mandibular lymph node.

The most common initial clinical signs included decreased appetite (16 [42%]), vomiting (14 [37%]), and diarrhea (5 [13%]), with many cats having > 1 clinical sign at the time of initial examination. Eighteen cats with cutaneous MCTs were initially examined only because of skin masses.

Results of a pretreatment CBC and serum biochemical profile were available for all cats. In addition, results of abdominal ultrasonography were available for 33 (87%) cats, results of thoracic radiography were available for 30 (79%) cats, results of cytologic examination of regional lymph node aspirates were available for 32 (84%) cats, results of cytologic examination of buffy coat smears were available for 25 (66%) cats, results of cytologic examination of bone marrow aspirates were available for 17 (45%) cats, and results of testing for FeLV and FIV infection were available for 33 (87%) cats (**Table 1**). Results of thoracic radiography were normal in 29 of 30 (97%) cats; 1 cat with MCT of the mesenteric lymph nodes had severe mastocytic pleural effusion. Cytologic examination of regional lymph node and bone marrow aspirates revealed MCT infiltration in 19 of 25 (75%) and 5 of 17 (29%) cats, respectively. None of the cats were seropositive for FeLV or FIV infection.

Previous treatment—The 6 cats with secondary cutaneous MCTs had undergone splenectomy because of splenic MCT between 1 and 8 months (median, 3 months) prior to treatment with lomustine. One cat with a gastrointestinal tract MCT had undergone resection of a solitary jejunal mass. The other cat with gastrointestinal tract MCTs had had 2 jejunal masses resected. Both cats with gastrointestinal tract MCTs had nonresectable regional lymph nodes that were positive for metastatic MCT. The 2 cats with hepatic MCT had undergone splenectomy because of splenic MCT 1 and 4 years prior to treatment with lomustine. Nineteen of the 38 cats were treated with prednisone before receiving lomustine, and 4 of the 19 (21%) had a partial response, with response duration ranging from 30 to 90 days. Seven of the 38 cats were treated with other chemotherapeutic agents before receiving lomustine, including vinblastine (n = 3), vinblastine combined with cyclophosphamide (1), vincristine (1), and chlorambucil (2). One cat treated with vinblastine had a partial response that persisted for 45 days. This same cat had previously responded to treatment with prednisone. All cats previously treated with prednisone or other chemotherapeutic agents had progressive disease before starting treatment with lomustine.

Table 1—Results of initial staging tests in 38 cats with MCT treated with lomustine.

		Tumor location					
		Skin		Mesenteric	Gastrointestinal		
Staging test	Test result	Primary*	Secondary†	lymph nodes	tract	Liver	Spleen
Abdominal ultrasonography							
	Normal	17	3	0	0	1	0
	Abnormal	0	2	6	2	1	1
	Not performed	3	1	1	0	0	0
Thoracic radiography							
	Normal	15	5	5	2	2	0
	Abnormal	0	0	1	0	0	0
	Not performed	5	1	1	0	0	1
Cytologic examination of lymph nodes							
	Negative	10	2	0	0	1	0
	Positive	6	2	7	2	1	1
	Not performed	4	2	0	0	0	0
Cytologic examination of buffy coat smear							
	Negative	9	0	4	1	0	0
	Positive	3	6	0	0	1	1
	Not performed	8	0	3	1	1	0
Cytologic examination of bone marrow aspirate							
	Negative	6	1	4	1	0	0
	Positive	2	3	0	0	0	0
	Not performed	12	2	3	1	2	1

Data are given as number of cats.
*Not associated with splenic MCT. †History of splenic MCT.

Lomustine treatment and toxicoses—For each individual cat, the attending clinician determined the number of lomustine treatments administered. In general, however, lomustine administration was continued beyond the first treatment cycle for as long as a response (complete or partial) was observed. A total of 121 lomustine treatments were administered to the 38 cats; median number of treatments was 2 (range, 1 to 12). Ten cats received 1 treatment; 10 cats received 2 treatments; 8 cats received 3 treatments; 1 cat received 4 treatments; 3 cats received 5 treatments; 2 cats received 6 treatments; and 1 cat each received 7, 8, 9, and 12 treatments.

Lomustine dosing interval was determined by the attending clinician on the basis of personal preference or results of hematologic testing or by owner compliance. Median interval between the first and second lomustine treatments was 6 weeks (range, 3 to 12 weeks). Median interval between lomustine treatments after the first treatment cycle was 4 weeks (range, 3 to 8 weeks).

Targeted lomustine dosage was 50 mg/m^2 in 22 cats and 60 mg/m^2 in 16 cats. The actual dose of lomustine administered was rounded to the nearest available capsule size, but in all cats, the actual dose administered was within 2.5 to 5 mg of the calculated dose. For 24 cats, this necessitated using reformulated 2.5-mg or 5-mg lomustine capsules. For all cats in the study, the median dosage of lomustine was 56 mg/m^2 (range, 48 to 65 mg/m^2). The median dose of lomustine was 15 mg (range, 10 to 20 mg). The median cumulative dosage of lomustine administered was 125 mg/m^2 (range, 49 to 691 mg/m^2).

Neutrophil counts were obtained weekly for 4 weeks after the first lomustine treatment in 19 cats. The time at which the nadir in neutrophil count occurred ranged from 7 to 28 days after treatment (median, 21 days). Median neutrophil count at the nadir was 2,600 cells/µL (range, 0 to 17,948 cells/µL); 3 (16%) cats had neutrophil count nadirs < 1,000 cells/µL (**Table 2**). Neutrophil recovery could be adequately evaluated in 9 cats. Neutropenia (neutrophil count < 2,500 cells/µL) lasted 7 to 28 days after the nadir (median, 7 days). None of the cats developed a fever or had clinical signs consistent with sepsis after treatment.

After the first lomustine treatment, the nadir of the platelet count could be determined in 11 cats; the median time at which the nadir in platelet count occurred was 14 days (range, 7 to 28 days). Median platelet count at the nadir was 201,000 platelets/µL (range, 42,000 to 545,000 platelets/µL); only 1 cat had a platelet count < 50,000 platelets/µL. Thrombocytopenia (platelet count < 200,000 platelets/µL) lasted 7 to 14 days after the nadir (median, 14 days). Except immediately prior to each successive lomustine treatment, neutrophil and platelet counts were rarely determined after treatments beyond the initial lomustine dose. Three cats had neutrophil counts < 500 cells/µL 7 days (1 cat) and 28 days (2 cats) after receiving a second treatment of lomustine at a dosage of 50 mg/m^2; neutrophil counts were not available after the first lomustine treatments in these cats.

Results of serum biochemical profiles were available for 25 cats given between 1 and 11 doses of lomustine (median, 2 doses). Median cumulative lomustine dose given to these cats was 120 mg/m^2 (range, 50 to 660 mg/m^2). Serum biochemistry profiles were performed within 1 month of the last lomustine dose in 8 cats, within 2 months in 15 cats, and within 4 months in 2 cats. One cat had abnormally high serum alanine transaminase activity (356 U/L; reference range, 29 to 186 U/L) after 3 lomustine treatments (cumulative dose, 180 mg/m^2); however, progression of hepatic MCT was also noted at the same time. No evidence of hepatic or renal dysfunction was detected in any of the other cats.

Self-limiting gastroenteritis was observed in 6 of 38 (16%) cats after the first lomustine treatment and 4 of 28 (14%) cats after the second lomustine treatment; all cats with adverse gastrointestinal tract effects had inappetence, vomiting, or diarrhea before treatment with lomustine.

One cat given 4 doses of lomustine (cumulative dose, 200 mg/m^2) and a second cat given 8 doses of lomustine (cumulative dose, 400 mg/m^2) developed severe pleural effusion. Results of echocardiography and analysis of the pleural fluid (modified transudate) were suggestive of right-sided cardiac failure in 1 cat. No diagnosis was obtained in the other cat.

Response to treatment—Nineteen of the 38 (50%; 95% CI, 35% to 65%) cats had a complete or partial re-

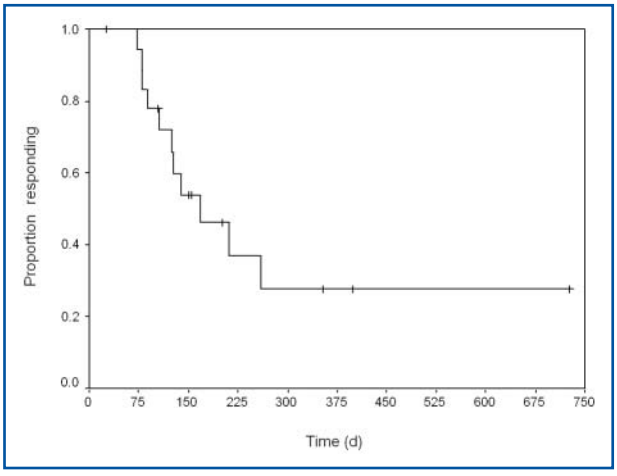

Figure 1—Kaplan-Meier curve of response time in 19 cats with MCT treated with lomustine. Median response duration was 168 days (95% CI, 78 to 258 days).

Table 2—Severity of adverse hematologic events following administration of the first dose of lomustine in cats with MCTs.

		Neutropenia grade						Thrombocytopenia grade				
Dosage (mg/m^2)	No. of cats	0	1	2	3	4	No. of cats	0	1	2	3	4
50	10	5	1	2	2	0	5	2	0	2	1	0
60	9	5	2	1	0	1	6	4	0	2	0	0

Grade 0 = ≥ 2,500 neutrophils/µL and ≥ 200,000 platelets/µL; grade 1 = 1,500 to 2,499 neutrophils/µL and 100,000 to 200,000 platelets/µL; grade 2 = 1,000 to 1,499 neutrophils/µL and 50,000 to 99,000 platelets/µL; grade 3 = 500 to 999 neutrophils/µL and 25,000 to 49,000 platelets/µL; and grade 4 = < 500 neutrophils/µL and < 25,000 platelets/µL.

Table 3—Classification of response to treatment with lomustine as a function of disease characteristics in 38 cats with MCTs.

Variable	Characteristic	Response		
		Complete	Partial	None
All cats		7	12	19
Anatomic location of tumor				
	Skin (primary)*	2	8	10
	Skin (secondary)†	0	0	6
	Mesenteric lymph node	2	3	2
	Gastrointestinal tract	1	1	0
	Liver	2	0	0
	Spleen	0	0	1
Previous chemotherapy‡				
	Yes	4	5	10
	No	3	7	9
Response to previous chemotherapy				
	Yes	2	1	1
	No	2	4	9
Lomustine dosage (mg/m^2)				
	50	4	5	13
	60	3	7	6

Data are given as number of cats.
‡Includes corticosteroids and other chemotherapeutic agents.
See Table 1 for remainder of key.

sponse following treatment with lomustine; the remaining 19 cats failed to respond. Median duration of the response was 168 days (range, 25 to 727 days; 95% CI, 78 to 258 days; **Figure 1**). Seven (18%) cats had a complete response, with median response duration of 211 days (range, 80 to 727 days; 95% CI, 34 to 387 days). Twelve (32%) cats had a partial response, with median response duration of 168 days (range, 25 to 399 days; 95% CI, 112 to 224 days; **Table 3**). All responses to lomustine occurred after the first lomustine treatment. Eleven (58%) cats had a relapse during the follow-up period. Eight (42%) cats were in remission at the conclusion of the study and were censored because they were lost to follow-up (n = 5) or died of unrelated causes (3). Median follow-up time for these 8 cats was 162 days (range, 25 to 727 days).

Nineteen cats did not receive any additional treatments after treatment with lomustine failed. In the remaining 19 cats, additional treatments were administered after treatment with lomustine failed. Nine cats were treated with vinblastine alone, 4 were treated with vinblastine combined with cyclophosphamide, 2 were treated with prednisone, 2 were treated with mechlorethamine, 1 was treated with chlorambucil, and 1 was treated with imatinib mesylate. One cat with hepatic MCT that had a complete response with lomustine treatment but relapsed had a complete response with mechlorethamine that persisted for 180 days. One cat with primary cutaneous MCT that failed to respond to lomustine treatment had a partial response that persisted for 90 days after administration of vinblastine in combination with cyclophosphamide.

Discussion

Results of the present study suggested that lomustine had antitumor activity in cats with MCTs when administered at a dosage of 50 to 60 mg/m^2 and was well tolerated. The response rate (50%) in the present study supports the use of lomustine for treatment of cats with MCTs in which local treatment is not possible or has not been successful.

Cats in which the target lomustine dosage was < 50 mg/m^2 were excluded from the present study because evaluating effects of chemotherapeutic agents delivered at the maximum tolerated dosage is a more appropriate indication of antitumor efficacy.[20] Results of a study[18] of cats with various tumors suggested that the response rate was higher when lomustine was administered at dosages at or close to the maximum tolerated dosage of 50 to 60 mg/m^2.

In the present study, 9 of the 12 cats with noncutaneous MCTs and 10 of the 26 cats with cutaneous MCTs had a complete or partial response following lomustine treatment. Surprisingly, all 10 of the cats with cutaneous MCTs that responded to treatment had primary cutaneous MCTs, and none of the 6 cats with secondary cutaneous MCTs had a response. Unfortunately, because of the small sample size, we were unable to perform statistical analyses to determine whether specific variables, such as anatomic location, were associated with tumor response. Thus, additional controlled studies of lomustine in cats with MCTs are required.

Mast cell tumors account for up to 21% of cutaneous tumors in cats.[21] Histologic grading and completeness of excision are not associated with the likelihood of recurrence or with survival time, and most investigators have concluded that most cutaneous MCTs in cats have a benign biological behavior.[2–5,7] In a study[3] of 32 cats that underwent surgical excision of cutaneous MCTs, for instance, local recurrence was observed in only 5 (16%). A lower recurrence rate (3%) was reported for 35 cats with cutaneous MCTs treated by means of irradiation with radioactive strontium.[6] Nevertheless, some cats with cutaneous MCTs are not suitable candidates for local treatment because of infiltration into the adjacent subcutis (eg, diffuse histologic subtype),[5] diffuse distribution within the skin (ie, miliary distribution),[1] or concurrent systemic involvement.[7] In the present study, 6 of the 26 (23%) cats with cutaneous MCTs had a history of splenic MCT (ie, secondary cutaneous MCT). Also, at least 6 of the 20 (30%) cats with primary cutaneous MCTs had metastases to local lymph nodes or bone marrow, suggesting that systemic chemotherapy was the most appropriate treatment modality. In a recent study,[7]

median survival time was significantly shorter in 6 cats that each had 5 or more localized cutaneous MCTs (375 days) than in 19 cats with single cutaneous MCTs (median not reached). Four of the cats with multiple MCTs died of mast cell neoplasia while only 1 of the cats with a solitary MCT died of the disease during the study period.[7] Future studies to evaluate lomustine as an adjunct treatment for cats with multiple MCTs are warranted.

Both of the cats with lymph node metastases from gastrointestinal tract MCTs in the present study responded to lomustine treatment. Mast cell tumor is the third most common primary intestinal tumor in cats, after lymphoma and adenocarcinoma.[1] Surgical resection is indicated when possible, but because gastrointestinal tract MCTs are commonly infiltrative or metastasize widely, there are few reports[10–12] of successful treatment. Treatment with lomustine, therefore, may be a useful alternative in cats with gastrointestinal tract MCTs.

Mast cell tumor is the most common tumor of the spleen in cats and accounts for 15% to 26% of all splenic diseases.[22,23] Splenectomy is the treatment of choice, and long survival times have still been reported following splenectomy in cats with evidence of systemic disease even without any other treatment.[13] The 6 cats with secondary cutaneous MCT in the present study had undergone splenectomy for splenic MCT between 1 and 8 months prior to treatment with lomustine, and no response to lomustine treatment was seen in any of these cats. Development of cutaneous MCTs[24] and recurrence of initial clinical signs (eg, vomiting and diarrhea)[13,25] after splenectomy have been previously reported, but factors associated with a poor response to splenectomy should be identified before the routine use of lomustine for this form of MCT is advocated.

The dose-limiting toxic effect of lomustine in cats is neutropenia.[17] Lomustine is commercially available as 10-, 40-, and 100-mg capsules, and reformulated capsules were required for half the cats in the present study for accurate dosing. The percentage of cats with severe neutropenia (neutrophil count < 1,000 cells/μL) was considered acceptable, and importantly, none of the cats developed signs of infection. Findings by Fan et al[18] suggest that cumulative myelotoxicity may occur in cats receiving lomustine long term. In the present study, evidence of progressive myelosuppression was not readily apparent, but hematologic data after the second and later lomustine treatments were limited. Some cats had multiple serum biochemistry profiles performed after lomustine administration, and evidence of organ toxicoses was not observed. However, the follow-up time might not have been adequate. For example, hepatic damage in dogs has been shown to be cumulative and might occur up to 49 weeks after the last dose of lomustine is administered.[16] Two cats in the present study developed pleural effusions after receiving multiple lomustine doses. Although an association with lomustine treatment was not confirmed, pulmonary fibrosis is a rare toxicosis in people receiving lomustine.[26] We currently recommend that cats treated with lomustine be carefully evaluated for cumulative myelosuppression and organ damage until additional information is available.

a. CeeNU, Bristol-Myers Squibb Co, Princeton, NJ.

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