

My Experience with Lomustine

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Lomustine (CCNU) is not considered a first-line chemotherapy agent by veterinary oncologists; it is usually used as a rescue drug when other protocols fail or relapse occurs. However, I have found it both successful and advantageous compared to other protocols for cats. Its use is almost free of side-effects; cats do not show lethargy, vomiting, and anorexia typical of more aggressive protocols. In addition, it is given orally about once per month.

The only significant side-effect is neutropenia. This occurs in about 40% of treated cats and only after several doses. It is also spontaneously reversible and should not call for specific treatment. Use of the drug can continue once the neutrophil count returns into the normal range. On a positive note, most cats that experience neutropenia are very likely to experience good response.

Other side effects noted are focal areas of hair loss, often multiple in the affected cats, slow regrowth of hair shaved for surgery, and infections due to immunosuppression. I have seen one case of severe coughing that was responsive to Clavamox, making it likely to be *Bordetella*. However, I have never seen immunosuppression leading to sepsis and other severe disease.

Successful treatment is defined as creating a clinical sign-free cat. Vomiting and/or diarrhea should stop. The appetite should return to normal, and lost weight should be regained. In my experience, remission occurs about 75% of the time in cats with small cell lymphoma after approximately six treatments. Currently, I recommend treatment with lomustine every 4 weeks until remission then every 6-8 weeks long-term. Treatment of lymphoblastic (large cell) lymphoma is not as successful as treatment of small cell lymphoma, but many of these cats respond surprisingly well to the same lomustine protocol used for small cell lymphoma.

It is not possible to clearly distinguish some cases of small cell lymphoma from IBD using cytology so a full thickness biopsy of the small bowel or stomach with histopathology is needed for accurate diagnosis. There are some ambiguous cases (5-10%) that require PARR testing (Michigan State University) for clear differentiation. Lymph node cytology is particularly problematic to distinguish IBD from small cell or lymphoblastic lymphoma; therefore, a wedge biopsy is recommended for lymph nodes. However, I do not routinely biopsy mesenteric lymph nodes because many cats with lymphoma of the bowel will not have lymphoma in the lymph nodes; the lymph nodes are read as lymphadenitis. In addition, treatment is the same whether it is in the lymph nodes or not.

Although my primary use of lomustine is for treating small cell lymphoma of the stomach or small bowel, cats with inflammatory bowel disease also respond well. Therefore, if the owner will not permit a laparotomy for full-thickness biopsy of the stomach or small bowel or if the cat is not healthy enough for biopsy, lomustine and prednisolone can be used for empirical treatment. This approach is definitely not my preferred way to manage these cats, but some situations make it an option to consider.

Many forms of mast cell disease also respond well to lomustine. If the spleen is involved, a splenectomy is indicated. If several cutaneous masses are present, excision is indicated. Otherwise, surgery is not part of the treatment. Lomustine is given using a similar protocol for lymphoma.

The official dose for lomustine is 50-60 mg/m². However, I dose on the low end of this range. It is commercially supplied as a 10 mg capsule, and I have had it compounded into 12, 9, and 6 mg capsules* and dosed according to the chart below. Prednisolone is given simultaneously at about 10 mg per cat q24h PO. Alternatively, an injection of 20 mg of Depo-Medrol is given with each dose of lomustine.

Lomustine should not be given at the prescribed dose if the neutrophil count is $2.5 \times 10^3/\text{mm}^3$ or less. If it is 2.0 to $2.5 \times 10^3/\text{mm}^3$, I give a reduced dose to the next lower category in the chart below. If it is less than $2.0 \times 10^3/\text{mm}^3$, I delay dosing for 2 weeks. If the neutrophil count increases to $2.5 \times 10^3/\text{mm}^3$ or more, I continue treatment. If not, the next dose is delayed until the neutrophil count is suitable. Interestingly, cats that have bouts of neutropenia often have the best response to treatment. It is advantageous to share this observation with owners so they do not get discouraged when neutropenia occurs.

The capsule is extremely sticky when moist so a clean pilling is necessary followed by a few milliliters of water orally to prevent adhesion to the esophagus. If the capsule gets wet, roll it in corn starch. That will dry it and leave it slick so it can be used again. The current cost is about \$10 per capsule when a bottle of 20 is purchased. It can be obtained on prescription at local pharmacies or thorough compounding pharmacies. The compounding pharmacy I use is about half that price.

Administering lomustine to fractious cats is best done by giving anesthesia or heavy sedation, intubating, and passing a feeding tube into the stomach. (A 12 Fr. red rubber tube works well.) Put the contents of the capsule in 5 ml of tap water in a 6 cc syringe, shake well, attach to the feeding tube, and syringe the lomustine-water into the stomach. Having an endotracheal tube in place keeps the feeding tube from entering the trachea and guarantees it will go into the stomach. If in the stomach, there will be only about 2-3 cm of tube exiting the cat's mouth. Follow with plain tap water to make sure the whole dose is given.

Most cats that respond will be significantly improved by the time of the third treatment. If this does not occur, one should re-evaluate the case to decide if further treatment is advisable.

When recurrence occurs following remission, lomustine has not been very successful for me as a rescue drug. Therefore, continuing treatment every 6-8 weeks on a long-term basis is preferable. If relapse occurs and the client wishes to continue, chlorambucil or the modified Wisconsin protocol should be considered. However, recurrence is usually a very aggressive form of disease so most owners will correctly elect euthanasia.

Dosing of Lomustine for Cats with Normal Neutrophil Counts

Body Weight in Kg	Mg of Lomustine
2.0-3.0	6
3.1-4.5	9
4.6-5.9	12
7 or more	15

*Compounded lomustine is available at Apotheca Compounding Pharmacy, 1-210-226-1112.