

## **Angiogenesis Inhibiting Therapy for the Treatment of Cancer in Animals** **Phyllis Ciekot Glawe DVM MS DACVIM (Oncology)**

### **Terminology:**

*Angiogenesis* refers to the formation of new blood vessels. This is a normal phenomenon in animals, however cancer cells capitalize upon this process to facilitate growth and *metastases* (spread to distant organs). Cancer cells can produce growth factors that stimulate angiogenesis, producing easier access to oxygen and food supply from the host. As the cancer cells grow in number, the invasion into the host's organs and tissues causes numerous problems, resulting in illness and eventually overwhelming the host's normal body functions. In recent years, there have been many exciting discoveries regarding treatments to stop this process. *Anti-angiogenesis therapy (also known as angiogenesis inhibiting therapy or metronomic therapy)* is used to cut off the blood supply to rapidly growing cancer cells.

### **What is Anti-angiogenesis therapy?**

Unlike chemotherapy, angiogenesis inhibiting therapies do not directly kill cancer cells. The medications are administered daily or every other day to create an environment that over time is less favorable for growth of cancer cells. This is essentially treating cancer like a chronic disease. Cancer cells may always be present, but in such small numbers that the host remains unaffected. Some of the oral medications are anti-inflammatory in nature, antibiotic treatments or low-dose oral chemotherapy agents. In veterinary medicine, this is a relatively new field of research, and new developments are still forthcoming. Not all angiogenesis inhibiting drugs work well in all species or for all cancer types.

### **What are the drugs most commonly used in veterinary medicine?**

A non steroidal anti-inflammatory medication (NSAID) **piroxicam** is one of the anti-angiogenesis therapies used in our practice. This drug is also used for pain management. An oral low dose chemotherapy agent, **cyclophosphamide (Cytoxan)** is the other medication commonly prescribed. Both medications are administered orally on a daily or every-other-day basis at home.

### **What are the side effects of piroxicam (also known as Feldene)?**

- 1) Piroxicam is a human drug typically available as a 10 mg capsule. Companion animals generally require a smaller size, thus necessitating compounding to a smaller size. This is generally performed by a pharmacy familiar with the compounding process.

- 2) This drug can be harmful to the kidneys. It is not recommended for patients with pre-existing kidney disease. Bloodwork including urinalysis is required for consistent monitoring of the patient to avoid any problems
- 3) Gastrointestinal side effects, such as nausea, vomiting, poor appetite, weight loss and ulceration resulting in bloody stools are important symptoms to watch for. To avoid this problem, piroxicam is administered with food, can be given with GI protectant therapy (such as pepcid or misoprostol) and NEVER can be administered concurrently with other NSAIDS such as Rimadyl, deramaxx nor oral steroids.
- 4) If any problems arise during the course of therapy, piroxicam will be discontinued. If there are ever any questions regarding side effects, contact us immediately.

### **What are the side effects of cyclophosphamide (Cytosan)?**

- 1) Cyclophosphamide is a human medication typically available in 25 and 50 mg size capsules. For low dose therapy, smaller doses are utilized, thus this drug must be compounded also for safe dosing.
- 2) Gastrointestinal side effects are rare at the low dose. Low white cell counts are uncommon, but also possible. (These can be problems at the higher doses prescribed for other cancer conditions)
- 3) Cyclophosphamide is a drug that can cause urinary bladder irritation. For this reason, monitoring of the urine is particularly important. If any indication of inflammation (cystitis) is noted during the course of therapy, this drug will be discontinued. Symptoms to watch for at home include frequent urination, blood in the urine, straining to urinate and licking of the penis/vulva.
- 4) Wear gloves when handling this medication for administration. If the medication contacts bare skin, there is the possibility that it can be absorbed through the skin.

### **How do we monitor for success of therapy?**

Simply monitoring for local recurrence or evidence of metastases with periodic physical exams, imaging tests (such as radiographs) or investigating any suspicious lesions are the methods utilized. There is no blood test typically used for monitoring for cancer recurrence.

### **How do we monitor for side effects from the medications?**

We recommend a baseline blood test and urinalysis followed by repeating these tests at one month following initiation of therapy. If your pet is tolerating the therapy well then we recommend an exam, bloodwork and urinalysis very 3 months thereafter. Our goal is to treat the patient's cancer safely, effectively and as easily as possible. If at any time, questions or concerns arise, do not hesitate to call us.