



The Pet Oncologist

FAQs - Metronomic Chemotherapy in Pets.



Your vet just recommended metronomic chemotherapy to treat your pet's cancer. What is metronomic chemotherapy? How does it work? What are the pros and cons? Here are some answers to some 'Frequently Asked Questions' about metronomic chemotherapy in dogs & cats.

What is metronomic chemotherapy?

Metronomic chemotherapy is the long-term daily or every second daily administration of lower than standard dosages of chemotherapy. In contrast to the administration of standard dosages of chemotherapy (i.e. conventional chemotherapy), which directly results in cancer cell kill, metronomic dosing of cyclophosphamide stimulates the immune response against cancer and suppress blood vessel growth associated with cancer. If cancer loses their blood vessel supply, it will eventually starve itself of oxygen and nutrients, and thus die.

How is it different from conventional chemotherapy?

Conventional chemotherapy is given at higher dosages, known as the maximum tolerated dosages, to kill cancer cells. The aim of conventional chemotherapy is to kill rapidly dividing cancer cells. However, both cancer and some normal cells share similar, rapidly dividing cell properties. Unfortunately, to kill cancer cells; some normal cells can be affected, leading to potential side effects to the rapidly dividing gastrointestinal tract and bone marrow (i.e. drops in white cell counts). These side effects are usually temporary and require regular breaks to allow for the normal cells to recover. Conventional chemotherapy is typically administered every one to three weeks.

What drugs are usually involved?

Cyclophosphamide is the chemotherapy drug most commonly used in metronomic protocols in people and pets. Metronomic therapy typically consists of a combination of three medications that are administered orally at home: cyclophosphamide, piroxicam and frusemide. Piroxicam is a non-steroidal anti-inflammatory drug used for pain relief but also has anti-cancer properties. Frusemide is a diuretic medication that administered at the same time as cyclophosphamide to facilitate urination and thus, decrease the risk of sterile haemorrhagic cystitis to <5%.

Other chemotherapy drugs that can be administered at low doses and daily or every second day, include chlorambucil, melphalan and lomustine (CCNU).

What are the pros and cons of metronomic chemotherapy, compared to conventional chemotherapy?

Metronomic therapy is an attractive treatment option for many owners because they can administer the drug orally to their pets at home, the risk of chemotherapy toxicity is low (around 5%), and the cost is relatively low, compared with other treatment options. Most of the side effects are usually attributable to piroxicam, and not to the actual chemotherapy drug itself.

However, the cons are that it is still chemotherapy and needs to be administered by pet owners safely at home. Once started, it is considered life-long therapy for as long as it helps treat your pet's cancer. Because it does not necessarily directly result in cancer cell killing, it can take an average of 6-12 weeks before a response occurs. Therefore, in pets with cancer that is growing very fast, there may not be enough time to see a response to therapy. Lastly, long-term usage may be associated with damage to the bone marrow (leading to drops in the white cell counts) and sterile haemorrhagic cystitis (which is a painful bladder condition characterised by signs of lower urinary tract disease without evidence of urinary tract infection). However, these side effects are uncommon.

It is important to be aware that even if the cancer does not go away but remains the same size (i.e. stable disease), this is considered a success if your pet continues to have a good quality of life.

The Pet Oncologist has a client handout entitled 'Handling Chemotherapy Medications at Home'. Please refer to this handout on tips on how to administer oral chemotherapy at home.

What cancers can metronomic chemotherapy be used on?

Many cancers have the potential to respond to metronomic chemotherapy. It can be considered in a situation where pets have unfavourable prognostic factors (such as metastasis [i.e. cancer spread]), when surgery or other forms of therapy are not possible, when pets have failed standard of care, or if owners wish to try an anti-cancer therapy that has a low toxicity profile and is affordable. Often, metronomic therapy is not considered the standard of care, but it can be helpful and as a 'trial and see' approach.

In dogs, the main indications are as follows:

- Low-grade soft tissue sarcomas where residual cancer cells remain (i.e. incomplete margins surgery), to delay the regrowth of the cancer.
- Splenic haemangiosarcoma.
- A particular type of lung cancer, called 'pulmonary carcinoma' that has evidence of cancer spread to other areas of the body.
- Bladder cancer.
- Indolent lymphoma.
- Chronic lymphocytic leukaemia.

Cats with cancer can also respond to metronomic chemotherapy, predominately sarcoma, carcinomas, multiple myeloma and low-grade lymphoma.

Metronomic chemotherapy can be safely combined with other anti-cancer therapies, such as Palladia® (toceranib), radiation therapy and some conventional chemotherapy drugs.

How frequent are the visits?

When I start with metronomic therapy, I typically recommend a recheck two weeks later, four weeks later, six weeks later, then every 2-3 months after that. Each visit will consist of a physical examination, cancer measurement, blood and urine tests, to ensure pets are responding and tolerating therapy.

What are the side effects?

Most pets that receive metronomic therapy (95%) experience no side effects.

Approximately 5% of dogs experiencing a side effect (usually mild and gastrointestinal signs). Most side effects (if picked up early) are managed with stopping the medications, reducing the dose, or the addition of supportive medications.

It is uncommon for a side effect to result in sterile haemorrhagic cystitis, long-term bone-marrow damage or hospitalisation (<5%).

If any gastrointestinal signs occur (such as diarrhoea, black tarry stools, vomiting or loss of appetite), it is usually due to piroxicam. These side effects typically resolve with temporarily stopping piroxicam and administering supportive care medications.