

# Oncology Tips: Metronomic Chemotherapy

## THE NEWEST TIPS AND TIDBITS FROM ONCOLOGIST DR. MANTOVANI!

- Tumor cells require formation of new blood vessels to grow past 2 mm in size, survive and metastasize. The main mechanism to acquire new blood supply utilized by cancer cells is angiogenesis, which occurs through the sprouting of new vessels from existing vasculature.
- Metronomic chemotherapy is given continuously at low doses, typically daily to every other day. It targets tumor endothelial cells and other components of the tumor microenvironment, therefore preventing angiogenesis. Metronomic chemotherapy also has immunomodulatory effects, such as decreasing regulatory T-cells.
- Can be utilized to treat various cancers in the gross disease and microscopic disease settings. The use of metronomic chemotherapy has been reported in veterinary oncology for soft tissue sarcoma, hemangiosarcoma, transitional cell carcinoma of the bladder and other multiple tumor types.
- Metronomic chemotherapy has the potential to slow down the progression of many cancers, and is continued long-term for as long as there is tumor control and no side effects. It is given orally and is relatively inexpensive, and therefore an attractive option in veterinary oncology.
- The most commonly used agents are cyclophosphamide and chlorambucil, in combination with a non-steroidal anti-inflammatory drug. Piroxicam has been commonly used in metronomic chemotherapy protocols, but has a higher side-effect rate. Therefore more selective COX-2 inhibitors, such as meloxicam and deracoxib, can be used instead of piroxicam. Metronomic chemotherapy is typically well tolerated, but side effects can occur:
- Metronomic cyclophosphamide can cause sterile hemorrhagic cystitis in approximately 30% of dogs, with a median time of onset after 4 to 5 months of therapy. Clinical signs include pollakiuria, hematuria and stranguria. Full urinalysis and urine culture should be performed in dogs with lower urinary tract signs receiving cyclophosphamide.
- Metronomic chlorambucil can cause thrombocytopenia with chronic use in up to 40% of dogs after 6 to 18 months of therapy, which can be irreversible in many cases. Continuous monitoring with monthly CBCs is indicated in dogs receiving this treatment, and therapy should be interrupted/discontinued if thrombocytopenia is seen.
- What about cats? Less investigated in cats, but use of metronomic cyclophosphamide has been reported. Azotemia likely due to NSAID administration is an important complication.



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