

# NEWS FROM THE WORLD OF ONCOLOGY

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## METRONOMIC THERAPY

Veterinary Oncology is a field that is consistently changing. Developments such as the use of the Melanoma Vaccine, the use of Palladia to treat mast cell tumours and the gradual emergence of the technology to allow for limited bone marrow transplantation are but a few of the more recent examples. A treatment that is becoming more and more wide spread is the use of metronomic therapy.



Metronomic therapy is targeted antiangiogenic therapy. Antiangiogenic therapy is treatment specifically targeted to prevent the formation of new vasculature. In order for tumours to grow, a rich blood supply must exist. Cancer cells have a difficult time with metabolism and growth if they are not located within about 1mm of a blood vessel. Thus the constant development of new blood vessels is essential to support the continued growth of a tumour. Therapy that could be directed towards stopping or delaying the development of new blood vessels would, in theory, provide a survival advantage in that tumour growth could be delayed or even prevented.

An ideal canine model for the evaluation of metronomic therapy has been hemangiosarcoma. This is a tumour of blood vessels and is an ideal candidate for metronomic therapy. Metronomics play an important role as an adjunctive and not primary therapy. This means that after definitive therapy with surgery and/or chemotherapy, metronomics can be used to prolong survival. Data from initial studies investigating the use of metronomic therapy in dogs with hemangiosarcoma support the use of this therapy. Dogs with hemangiosarcoma who are treated with surgery and chemotherapy have a survival time in the range of 6 months. However, dogs given metronomic therapy following standard chemotherapy and surgery have survival times approaching one year. This is a significant improvement over the previous therapy.

Other tumours appear to benefit from the adjunctive use of metronomic therapy. A recent study published in the Journal of Veterinary Internal Medicine investigated the use of metronomic therapy as adjunctive treatment for incompletely resected soft tissue sarcomas. This study demonstrated that when metronomic therapy was used in dogs with incompletely resected STS, the disease free interval (the time between surgery and tumour recurrence) increased from 211 days to over 410 days. This was a statistically significant improvement.

Many agents have been investigated for inclusion in metronomic therapy protocols. Currently most protocols utilize standard doses of COX-2 inhibitors and low doses of alkylating chemotherapy agents. Alkylating agents are used at doses well below cytotoxic levels and for this reason essentially do not result in the development of side effects. Therapy is best applied on a daily basis. For some animals therapy must be applied at decreased frequency due to medication sizes. Metronomic therapy is applied orally. A new development in metronomic therapy is the potential use of the recently developed tyrosine kinase inhibitor, Palladia. This medication, currently used to treat recurrent high-grade mast cell tumours, is known to inhibit vascular endothelial growth factor (VEGF). VEGF is a key component in the development of tumour vasculature and inclusion of Palladia in future metronomic therapy protocols seems almost certain.

Metronomic therapy is rapidly finding an expanded role in veterinary oncology. Its use is likely to expand as more and more studies are completed, demonstrating survival advantages in patients treated with this new and evolving therapy.

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