

Metronomic Chemotherapy

If you've ever been a musician, then you have probably heard of the metronome, a musical instrument that produces regular, metrical ticks representing a fixed, regular aural pulse. Metronomic chemotherapy is the term given to a protocol that uses low doses of oral chemotherapy given on a frequent basis at doses below the maximum tolerated dose (MTD) or conventional chemotherapy) with no prolonged drug-free period. With conventional chemotherapy, drugs are given in cycles at the MTD alternating with a drug-free period to allow for the patient to recover from adverse drug reactions on the bone marrow or gastrointestinal system. Fortunately, in our pet patients, we do not see side effects in the grand majority of our patients even with this protocol. However, there comes a time when conventional chemotherapy is not going to be effective and we need to redirect our therapeutic target.



Metronomic chemotherapy leads to sustained plasma concentrations of drugs targeting endothelial cells in the growing vasculature (anti-angiogenesis) without significant risk of toxic side effects. One of the greatest benefits for both our clients and our patients is the ability to administer all medications at home instead of having to make regular trips to the clinic for treatment. Aside from anti-angiogenic properties, research has shown these protocols to also activate the immune system, induce tumor dormancy and senescence, and affect the microenvironment of the tumor. The main effect of metronomic chemotherapy in activating the immune system is through the downregulation of regulatory T cells. Regulatory T cells are upregulated in cancer patients which causes inhibition of antigen-specific immune responses; thus, inhibiting anti-tumor immune responses that are carried out by cytotoxic and helper T cells.

It is often music to a client's ears when we are able to provide hope when it seems like all hope may be lost. Metronomic chemotherapy can be utilized in a number of situations including following surgery for an incompletely excised soft tissue sarcoma, when metastatic disease is diagnosed, and even when a tumor cannot be removed or the owner cannot afford more aggressive treatment options. The two mainstays of drugs are the combination of a non-steroidal anti-inflammatory medication (such as our headliner, piroxicam) and an alkylating chemotherapy drug (such as cyclophosphamide or chlorambucil). Given one of the main targets of Palladia is vascular endothelial growth factor (VEGF), this drug is used as a primary antineoplastic and can also be used as part of metronomic chemotherapy. VEGF and the receptors they bind to are the primary players in the process of angiogenesis making them a great target for metronomic chemotherapy.

One study that showed proof of the metronomic concept was reported last year. In the study, dogs with macroscopic soft tissue sarcomas were treated with a hypofractionated radiation protocol in which they received 5 treatments over 2 and a half weeks. Twenty of fifty (40%) of the dogs received metronomic chemotherapy following the radiation protocol. The addition of metronomic chemotherapy for these 20 dogs increased their overall survival times significantly to 757 days from 286 days for those without metronomic chemotherapy.



For patients with progressive/advanced disease or if there are financial constraints that preclude the use of more effective treatment options (like radiation therapy or a second surgery), the show can go on with metronomic chemotherapy as an option.

**By Zachary Neumann, MS Diplomate,
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SEVO-Med and PetCure Oncology co-hosted a free continuing education event in September at Maggiano's Little Italy at the St. Johns Town Center. The event garnered 40 attendees, including both veterinarians and technicians. The four-hour course included presentations on Stereotactic Radiosurgery (SRS) presented by Dr. Neal Mauldin; Feline Diabetes Mellitus presented by Dr. Krysta Deitz, Maddening Mast Cell Disease presented by Dr. Jennifer Locke, and Inflammatory Bowel Disease vs Lymphoma co-presented by Dr. Abigail Bertalan and Dr. Zachary Neumann. Thank you for attending! We hope that you found the event informative as well as enjoyable.



To learn more about upcoming CE events, visit PetCureOncology.com or SEVOMed.com!



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Due to the devastating effects of Hurricane Irma, we added a fundraising aspect to our event to support the Safe Animal Shelter in Middleburg. While all animals were saved, the facility suffered horrific water and structural damage due to the storm. The veterinary community was ready to support efforts to rebuild, and attendees who participated in the continuing education event with us raised \$850 to directly benefit Safe Animal Shelter. The generous gift from veterinarians in the community will allow the shelter to address the damage and they hope to reopen within 5-6 months. A HUGE thank you to everyone who participated in the event and donated!