Masitinib as a chemosensitizer of canine tumor cell lines

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Introduction: We recently showed that masitinib, a tyrosine kinase inhibitor targeting c-Kit, PDGF receptor and FGFR3 and affecting the FAK pathway, is safe and effective for the treatment of grade II or III nonresectable or recurrent mast cell tumors in dogs. To investigate the possible use of masitinib in combination with chemotherapy in dogs, we examined its ability to sensitize canine cancer cell lines to doxorubicin, vinblastine, and gemcitabine

Methods: A variety of canine tumor cells were incubated for 72 h with varying concentrations of chemotherapeutic agent +/- masitinib. Relative viable cell number was then determined using a commercial bioreductive fluorometric assay, expressed as a percentage versus untreated cells, and 50% inhibitory concentration calculated using nonlinear regression, fitting the data to a sigmoidal dose-response curve.

Results: Masitinib demonstrated a potent single-agent antiproliferative activity against OSW canine T-cell lymphoma. Masitinib (1-10 µM) sensitized all evaluated cell lines to doxorubicine (2- to 10-fold reduction in IC50), strongly sensitized DH82 histiocytic sarcoma cells to vinblastine (>74-fold reduction), and strongly sensitized D17 and Abrams osteosarcoma and CMT12 and CMT27 mammary carcinoma cells to gemticabine (>10-fold reduction).

Conclusion: Masitinib can chemosensitize canine tumor cell lines to the antiproliferative effects of multiple antineoplastic drugs at clinically achievable concentrations. The OSW canine T cell lymphoma cell line demonstrates unique sensitivity to masitinib through an as-yet unknown mechanism. The encouraging data presented here strongly justify clinical evaluation of masitinib / chemotherapy combinations in dogs with spontaneous tumors.