Canine Mast Cell Tumors

WSAVA Global Veterinary Community

Receptor tyrosine kinases (RTKs) are dysregulated in cancer and can sometimes result in uncontrolled growth and tumor progression. The RTK KIT is a major focus of research into canine mast cell tumors (MCTs), whereas other RTKs (eg, vascular endothelial growth factor receptor [VEGFR], platelet-derived growth factor receptor [PDGFR]) are not studied as frequently. This study evaluated expression and activation (phosphorylation) status of KIT, VEGFR2, and PDGFRs (α and β) and examined their associations with various clinical outcomes in canine MCTs. MCT biopsies, cultured mast cells, and surgical margin skin were analyzed for evidence of RTK expression and activation (phosphorylation), c-*KIT* mutational status, and KIT cellular localization pattern.

Heterogenous expression profiles for all 3 RTKs were found in the 27 tumors evaluated; expression varied in intensity and activation status. Phosphorylated KIT, VEGFR2, and KIT cellular localization were predictive of decreased survival time, disease-free interval, and increased metabolic rate. VEGFR2 and KIT diffuse cytoplasmic labelling were also significantly associated with increased rate of local recurrence.

This study demonstrated that phosphorylated KIT, KIT, VEGFR2, and PDGFRβ, as well as KIT localization, may be useful when selecting patients amenable to RTK inhibition and may serve as prognostic markers.

Global Commentary

Tyrosine kinase inhibitors (TKIs) such as toceranib and masitinib are important tools in the armamentarium against high-grade and high-stage MCT, in addition to conventional maximally tolerated dose protocols such as prednisone–vinblastine or prednisone–lomustine. c-*KIT* mutation analysis is the most commonly used method to determine if TKIs are an appropriate treatment. However, some patients without c-*KIT* mutations respond to TKI therapy. Examination of phosphorylated KIT, VEGFR2, and PDGFR status, although potentially useful in identifying good candidates for TKI therapy, are not yet routinely available from most veterinary pathology laboratories. The most consistent method to determine candidacy for TKI is c-*KIT* mutation analysis.—*Kelvin Kow, DVM, MS, DACVIM (Oncology), MRCVS, RCVS Recognized Specialist in Veterinary Oncology*

Source

Thompson JJ, Morrison JA, Pearl DL, et al. Receptor tyrosine kinase expression profiles in canine cutaneous and subcutaneous mast cell tumors. *Vet Pathol*. 2016;53(3):545-548.