A tyrosine kinase inhibitor targeting c-Kit for chronic inflammatory diseases involving mast cells

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2009 North American Veterinary Dermatology Forum (April 15-18, 2009 – Savannah, GA, USA)
Veterinary Dermatology 20(3): 216

Mast cells are involved in normal immune reactions, as well as pathological reactions observed in chronic inflammatory diseases, such as atopic dermatitis, asthma, irritable bowel syndrome and rheumatoid arthritis. Inhibitors of the c-Kit receptor, the growth factor receptor involved in the proliferation, differentiation and degranulation of mast cells, may have a beneficial influence on these diseases. Last year we reported that masitinib, a c-Kit inhibitor recently approved for the treatment of canine mast cell tumors, showed promising efficacy in canine atopic dermatitis with significant improvements measured by surface of lesions, CADESI and pruritus score.

Here we provide results from several in vivo models of chronic inflammatory diseases in mice, showing that masitinib may improve symptoms in these pathologies by reducing the abnormal inflammatory reaction.

In a model of allergic airway inflammation of Balbc mice sensitized to ovalbumine, masitinib (administered twice daily at 25 or 100 mg/kg/day after the sensitization process) diminished the airway hyper responsiveness during a methacholine challenge test (measured by the bronchconstrictive response) and markedly reduced the number of eosinophils in the bronchoalveolar lavage fluid.

Similarly, in a model of dextran sodium sulphate-induced colitis in Balbc mice, masitinib significantly reduced macroscopic and histological lesions, colonic concentrations of myeloperoxydase (MPO) and inflammatory cytokines.

Finally, in a model of rheumatoid arthritis in K/Bx TCR transgenic mice, masitinib dramatically reduced ankle thickening and significantly improved the arthritis score.

Together with clinical data in atopic dermatitis, these preclinical data suggest a beneficial impact of masitinib, in chronic inflammatory disorders involving mast cells.