Potential Novel Treatment for Canine Pemphigus Foliaceus

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In the literature

Goodale EC, White SD, Bizikova P, et al. Open trial of Bruton's tyrosine kinase inhibitor (PRN1008) in the treatment of canine pemphigus foliaceus. *Vet Dermatol.* 2020;31(5):410-e110.

FROM THE PAGE …

This study* evaluated the efficacy of a Bruton's tyrosine kinase (BTK) inhibitor in the treatment of canine pemphigus foliaceus. BTK is necessary for B-cell development, and autoreactive B cells are particularly dependent on BTK for survival as compared with normal B cells.[1] Autoreactive B cells produce autoantibodies, which contribute to various autoimmune diseases. Canine pemphigus foliaceus is characterized by production of antibodies directed primarily against desmocollin-1, a component of desmosomes. When BTK is absent, autoantibodies are lost and total antibody levels are unchanged. Because of this targeted effect, BTK inhibition is an appealing candidate in the treatment of humorally mediated autoimmune diseases (eg, pemphigus foliaceus).

The BTK inhibitor, BTKi PRN1008 (also called rilzabrutinib), was evaluated in the treatment of 4 dogs with pemphigus foliaceus. Initial doses of 15 mg/kg PO once daily were used, with administration increased to twice daily if inadequate response was noted. Final daily doses were in the range between 17 mg/kg and 33 mg/kg. All dogs showed improvement within the first 2 weeks of treatment, and 3 dogs were near remission by 20 weeks. The remaining dog achieved a fair response. After treatment, anti-desmocollin-1 immunoglobulin G was measured and determined to be absent in 2 dogs, reduced in 1 dog, and uninterpretable in 1 dog. An 8-year-old intact female developed pyometra during the study, but it is not clear whether this was related to rilzabrutinib. The same dog had elevated ALT and AST, both of which returned to normal when the dose was decreased.

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… TO YOUR PATIENTS

Key pearls to put into practice:

1. Pemphigus foliaceus is a challenging disease to treat. In most cases, high doses of systemic steroids are needed to induce remission. This is typically followed by a gradual dose reduction to the lowest steroid dose that maintains remission of disease. Frequently, nonsteroidal immunosuppressive drugs are also used to allow further reduction of the steroid dose.
2. Steroids have a variety of common adverse effects, which can be challenging to manage, especially in patients that require ongoing immunosuppression, as is the case in most dogs with pemphigus foliaceus. Nonsteroidal immunosuppressive drugs also have the potential for serious adverse effects. Thus, there is a need for novel targeted therapies in dogs with pemphigus foliaceus.
3. Rilzabrutinib is promising, as it was able to induce remission in 3 of the 4 study dogs. There were few adverse effects, but the study was limited by the small number of dogs enrolled. In addition, the study took place over 20 weeks, but most dogs with pemphigus foliaceus require ongoing, lifelong therapy. It is not known whether longer courses of rilzabrutinib may be associated with more adverse effects. Further study will be needed to determine if rilzabrutinib is a good long-term alternative to steroids in the treatment of pemphigus foliaceus.

Reference

1. Crofford LJ, Nyhoff LE, Sheehan JH, Kendall PL. The role of Bruton's tyrosine kinase in autoimmunity and implications for therapy. *Expert Rev Clin Immunol*. 2016; 12(7):763-773.