ACVIM FORUM 2019
Phoenix, Arizona
June 6-8, 2019
Specialty Symposium June 5
Innovation, Science + BEYOND

Controlled, Randomized Study of Intratumoral Tigilanol Tiglate (EBC-46) for Treatment of Canine Mast Cell Tumors

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Mast cell tumors (MCT), the most common skin malignancy in dogs, can pose treatment challenges for several reasons. With only one currently approved therapeutic for MCT in the US, development of additional treatment options is important to advancing clinical management.

Tigilanol tiglate, isolated from the Australian rainforest plant *Fontainea picrosperma*, possesses antitumor activity and stimulation of enhanced wound healing of the treatment site via activation of protein kinase C. Tigilanol tiglate may be effective when injected intratumorally as treatment for canine cutaneous or subcutaneous MCT.

One hundred twenty-three dogs with cutaneous or lower limb subcutaneous MCT confirmed by fine needle aspiration cytology were enrolled in the study. Dogs were randomized 2:1 to treatment with a single intratumoral injection of tigilanol tiglate or to sham treatment (untreated controls) in an investigator- and owner-masked multicenter study. The primary efficacy outcome was complete response (CR; disappearance of the target lesion) on Day 28. Other outcome measures included wound healing, tolerability, safety and health-related quality-of-life (HRQoL). Treated dogs with less than CR could receive a second intratumoral injection of tigilanol tiglate on Day 30 and untreated dogs could be crossed over to treatment with tigilanol tiglate on Day 30.

One hundred eighteen dogs were evaluable. Sixty of 80 dogs (75%) randomized to treatment with tigilanol tiglate achieved CR after a single intratumoral injection compared with 2 of 38 untreated dogs (5.3%) by Day 28 ($P < 0.0001$). Eighteen of the 20 treated dogs not achieving CR received a second intratumoral injection. Eighty-seven percent (68/78 evaluable) of treated dogs achieved CR within the possible two-dose treatment strategy. Ninety-six percent (55/57) of evaluable dogs achieving CR after first injection remained tumor-free at post-treatment day 84.

Of the 38 dogs randomized to the untreated control group, 33 were crossed over to intratumoral tigilanol tiglate and 62.5% (20/32 evaluable) achieved CR by Day 28 and 44.4% (9/20) of these remained tumor-free at post-treatment day 84.

Wounds developed in 92.5% (74/80) of dogs treated with tigilanol tiglate and healed rapidly from Day 7. Wound development is anticipated pathology associated with the mechanism of action of the drug. The most frequent adverse events were transient reactions at the treatment site. Owners indicated that overall HRQoL of treated dogs was similar to that of untreated dogs.

Tigilanol tiglate was highly effective for the treatment of cutaneous and lower limb subcutaneous MCT in dogs and was well tolerated with manageable side effects. Tigilanol tiglate has potential to play an important role in expanding treatment options available for dogs with MCT in both primary care and specialty settings.

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