ALTERNATING RABACFOSADINE/DOXORUBICIN:
Efficacy and Tolerability in Naïve Canine Multicentric Lymphoma

Lymphoma is one of the most common canine cancers. While capable of inducing remission in most naïve canine lymphomas, CHOP-based standard-of-care therapies can be cumbersome, owing to the number and frequency of treatments required (typically 12-16 visits over 15-25 weeks). Single-agent doxorubicin (DOX) is an alternative chosen by some for issues of convenience and/or cost, although it is considered inferior to CHOP in terms of efficacy. Rabacfosadine (TANOVEA™/VDC-1101/GS-9219), a novel double prodrug of the acyclic nucleotide phosphonate 9-(2-phosphonylmethoxyethyl)-guanine (PMEG), preferentially targets lymphoma cells with reduced systemic toxicity compared to PMEG. Single-agent rabacfosadine has been administered on a variety of dosing schedules to dogs with lymphoma. Objective response rates of 60-100% have been reported in previous studies, with improved outcomes in naïve patients. Given the convenience of an every-21-day administration schedule and non-overlapping mechanism of action/resistance with DOX, we sought to evaluate the efficacy and tolerability of treatment with alternating doses of rabacfosadine and DOX in dogs with naïve multicentric lymphoma.

Dogs with cytologically or histologically confirmed and immunophenotyped lymphoma were treated with alternating doses of rabacfosadine (1.0 mg/kg free base as a 30-minute IV infusion weeks 0, 6, 12) and DOX (30 mg/m2 weeks 3, 9, 15). Dogs experiencing a complete response (CR) received up to six total treatments, followed by monthly rechecks. Complete clinicopathological assessment and clinical assessment of remission and adverse effects (AEs) were performed every 21 days. Response was assessed according to published VCOG criteria and AEs according to the VCOG-CTCAE v1.1.

Thamm D, Vail D, Post G, Fan T, Phillips B, Elmslie R, Bechtel S, Klein M. 2016 ACVIM Forum Research Report Program. J Vet Intern Med, 31: doi:10.1111/jvim.13963.

54 dogs were prospectively enrolled. 51 were evaluable for response assessment and 52 were evaluable for progression free interval (PFI) and AE assessment. 44 dogs had B cell lymphoma and 8 had T cell lymphoma. 40 were considered substage A and 12 substage B. The overall response rate (ORR) was 81% (62% CR, 19% PR). The overall median PFI was 200 days (218 days for dogs experiencing CR and 148 days for PR). Both ORR and PFI were significantly higher in dogs with B cell lymphoma than in T cell (91% vs 25% and 215 vs 43 days). When compared with historical data, the observed overall PFI is superior to that reported with single-agent DOX (81-169 days) and comparable to that reported with standard 15-25 week CHOP protocols (140-219 days).

The majority of AEs were mild and self-limiting: gastrointestinal and hematologic AEs were most common. Grade 3 AEs included neutropenia (8), weight loss (6), hyporexia (4), diarrhea (4), liver enzyme elevations (3), thrombocytopenia (1), and dermatopathy (1). 5 dogs experienced grade 4 hematologic toxicity, and 1 developed transient grade 4 ALT elevation. 12 dogs experienced grade 1/2 dermatologic AEs, and 2 dogs developed grade 5 pulmonary fibrosis, several months after treatment discontinuation and while in CR. Modified ECOG performance status was generally maintained throughout the study. Rabacfosadine dose reductions were performed in 8 dogs and DOX dose reductions occurred in 6 dogs. No dose delays were required.

In conclusion, an alternating every-three-week rabacfosadine/DOX regimen was generally well tolerated and appears to result in outcomes comparable to those observed after standard CHOP-based protocols, with substantially fewer treatment visits (6 vs. 12-16). Adverse events were generally mild and self-limiting. Further studies are warranted to explore the impact of re-treatment as well as other rabacfosadine combinations.

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LATE-BREAKING ABSTRACT PRESENTATION

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Saturday, June 11 – 8:25-8:50 am

Colorado Convention Center, Mile High Ballroom 1B

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Tanovea™ (rabacfosadine) is not approved for companion animal use.