Regenaflex-K9 Safety Study: Managing Canine Lameness

Objective:

The study is designed to assess the safety and clinical response of dogs with clinical signs associated with lameness after intramuscular administration of Regenaflex-K9.

Study Design:

The study is an open label, unblinded, uncontrolled study in 25 dogs with clinical lameness. Twenty-five (25) dogs determined to have clinical lameness in one or more joints based on physical and radiographic examinations were enrolled. All dogs received a single dose of Regenaflex-K9 intramuscularly on Day 0. All dogs were included in the safety assessment which included reporting any adverse events occurring at any time during the study period. Dogs were assessed for multiple outcome measures including lameness based on a modified AAEP lameness scale (0-5), pain on flexion/manipulation of the affected joint(s) (0-5), and a multi-part visual analog scale (VAS) owner assessment of wellbeing or disability. The VAS used a 1-10 scale for 4 criteria: general activity level, overall pain, ability to walk/run, and ability to rise from laying down (1= normal for that dog, 10= inactive, very painful, unable to walk/run, and unable to rise from laying down). The individual scores were summed and averaged. Lameness scores and pain on flexion/manipulation were assessed on study Days 0, 7, 14, 30, and 60. Owner VAS was assessed on Days 0 and 30.

Success was established as an improvement in lameness and/or pain of 1 grade or more on Day 60.

Results:

Safety was assessed in all 25 dogs, including all adverse reactions noted during the study period. This included, but was not limited to, changes in body temperature, heart rate, and respiratory rate (TPR), and injection site reactions. No clinically significant changes in TPR were noted in 25/25 (100%) of the dogs. Mild, transient injection site swelling (4-hour and 12-hour duration) was observed in 2/25 (8.0%) of the dogs.

Lameness was assessed in 24/25 dogs on Day 60. One dog was not assessed beyond Day 30 (protocol deviation) and was excluded from outcome assessment. Of the remaining 24 dogs, 22/24 (91.7%) were successes, with 3/22 (13.7%) improving 1 grade, 14/22 (63.6%) improving 2 grades, and 5/22 (22.7%) improving 3 grades. On Day 60 4 dogs were grade 0 and 8 dogs were grade 1. Two dogs (8.3%), one an initial grade 3 lameness and the other a grade 4 failed to improve 1 degree. Pain was assessed in the same 24/25 dogs as included in the lameness evaluation. Of the 24 dogs, 24/24 (100%) improved at least 1 grade, with 5/24 dogs (20.8%) improved 1 grade, 13/24 (54.2%) improved 2 grades, 5/24 (20.8%) improved 3 grades, and 1/24 (4.2%) improved 4 grades. [Dog #19 was the protocol deviant, on Day 30 had improved 3 grades in both lameness and pain but is not included in the analysis.] The limbs affected in the study were 3 left front, 5 right front, 10 left hind, and 12 right hinds. Five dogs had multiple limbs affected. There was no apparent correlation between limb affected and outcome.

The owner VAS was assessed in 25/25 dogs on Day 30. Of the 25 dogs, 2/25 (8.0%) improved 2 grades, 2/25 (8.0%) improved 3 grades, 5/25 (20.0%) improved 4 grades, 7/25 (28.0%) improved 5 grades, 7/25 (28.0%) improved 6 grades and 2/25 (8.0%) improved 7 grades. At the end of the assessment period on Day 30 8/25 (32.0%) were grade 0 and 5/25 (20.0%) were grade 1.

Discussion:

After a single dose of Regenaflex-K9 only 2/25 (8.0%) dogs had a mild, transient swelling at the injection site. There were no systemic adverse events reported. Lameness improved at least one grade in 22/24 (91.7%) of the dogs, pain on manipulation of the affected limb in 24/24 (100%) of the dogs; both meet the criteria for a success. The owner assessment VAS demonstrated that 25/25 (100%) of the dogs' quality of life/disability improved after one dose of Regenaflex-K9.

As a comparison we can look at the results used in the clinical efficacy study for the FDA-CVM approval of Adequan® Canine, a product that is used in a similar fashion for the same clinical problem. The label indication is: Adequan® Canine is recommended for intramuscular injection for the control of signs associated with non-infectious degenerative and/or traumatic arthritis of canine synovial joints. The study was blinded and controlled, as all FDA-CVM trials must be. Dogs presented to the investigators with lameness and pain secondary to radiographically detectable traumatic or degenerative joint diseases in 1 or 2 joints were eligible for the study and were randomized into control and treated groups. The treated dogs received two doses of Adequan® Canine intramuscularly weekly for 4 weeks, a total of 8 doses. Placebo dogs received the equivalent volume of saline solution.

The final data analysis included data from 71 limbs in 51 dogs. Of these, 35 limbs in 24 dogs were in the Adequan® Canine treated group, and 36 limbs in 27 dogs were in the placebo treated group. The joints evaluated included hips, stifles, shoulders, hocks, and elbows. Interestingly, the time course for the study is not included in the results. At the interim time point of the study, 37% of the placebo group were responders (successes), and 50% of the treated dogs were responders. At the end point, 33% of the placebo and 67% of the treated were responders. In most studies evaluating the response of any group- people, horses, dogs- to disease modifying osteoarthritis drugs (DMOADs) there is a placebo responder rate of approximately 40%. There were 4 adverse clinical events reported, including bleeding which is an acknowledged problem with this class of drugs- they are in the same family as heparin.

While a larger randomized, controlled, blinded study is needed to make more definitive claims, and a pilot version of that study is underway, these results appear to demonstrate clinical benefits of Regenaflex-K9 for managing lameness in dogs with a lack of significant adverse events.