Clinical Trial of ASO Treatment in DM Affected Dogs

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The purpose of this study is to evaluate the efficacy of a promising new drug as a treatment for DM with hopes to slow disease progression. Dogs will be administered an antisense oligonucleotide (ASO) that will repress the production of the mutant protein, superoxide dismutase 1 (SOD1). The ASO has been tested in a preclinical setting for safety in dogs. The drug will be injected into the spinal fluid at the low lumbar region of the spinal cord. The study will be randomized and double blinded; meaning the investigator and the pet owner will not know whether the dog receives the drug. Eight dogs will receive the drug and 4 dogs will receive the vehicle. Based on the randomization design, your dog has a 67% chance of receiving the therapy.

We will monitor clinical disease progression and evaluate cerebrospinal fluid, brain MRI and a new electrodiagnostic technique, motor unit number estimate (MUNE). This technique has been used extensively on ALS patients in order to monitor and predict disease progression. We would like to use this same technique with brain MRI on DM-affected dogs for monitoring disease progression and to evaluate for efficacy of the therapeutic.

INCLUSION CRITERIA BELOW MUST BE MET TO BE CONSIDERED FOR STUDY

History

Slowly progressive loss of coordination over 1-3 months, no signs of waxing or waning, and the owners do not perceive their dog to be in discomfort

Neurologic Examination

EARLY DISEASE: Progressive asymmetric general proprioceptive ataxia that is considered mild.

Breeds Included

Boxers approximately 9 years of age or older at the time of initial examination
Pembroke Welsh Corgis approximately 10-11 years of age at the time of initial examination
Other breeds older than age of 9 years old at the time of initial examination

Diagnostic Testing (Performed by a board-certified veterinary neurologist: www.acvim.org)

No significant abnormalities on bloodwork, thoracic radiographs and abdominal ultrasound
Genetic testing results for SOD1:c.118A mutant homozygotes (A/A -- AT RISK)
Normal entire spinal cord MRI (cervical, thoracic, lumbar, sacral)
Normal CSF analysis
Normal electrodiagnostic testing results

Treatments and Follow-up Testing
An informed consent will be signed by the owner and Dr. Coates. The owner must be compliant and return to the MU VMTH or to their board-certified veterinary neurologist once a month for repeat injections of the drug (under anesthesia) into the spinal fluid. Follow up electrodiagnostic testing and MRI (at MU VMTH) will overlap with the treatment every 3 months.

Necropsy Confirmation
Following death or at time of euthanasia, the dog will need to be brought to MU VMTH for necropsy. A histopathologic confirmation of DM is required.

THE CANDIDATE DOG MUST BE ABLE TO COME TO THE UNIVERSITY OF MISSOURI FOR BASELINE TESTING, EVERY THREE MONTHS THEREAFTER AND AT THE TIME OF EUTHANASIA. It is easiest if you are within driving distance but we can work with a board-certified neurologist to administer once a month injections into the spinal fluid.