

Lay Summary of Nikkomycin Z Preclinical Dog Study

Valley Fever is a significant problem in dogs as it is in people. In contrast to humans, it appears that most of the dogs that become ill enough to see a veterinarian require treatment with medication. Courses of treatment are usually long, 6-18 months for cases without complications, sometimes years for recalcitrant or recurrent cases. Some cases fail to respond to the currently available medications and we either have to explore more dangerous treatments or there are no treatments left to try on the dogs. Newer medications that shorten treatment time and provide potential cure of the disease are needed to treat both humans and dogs.

Nikkomycin Z is a drug that has shown the potential to cure mice experimentally infected with Valley Fever. This drug has been tested for safety in mice, rats, and dogs and has produced few adverse effects. A Phase I safety study has been done in humans and a preclinical efficacy study in dogs is being planned herein. A Phase II study is the first look at whether a new drug is effective for the disease, in this case Valley Fever. The Valley Fever Center for Excellence has just been awarded \$3 million to make more drug and begin the Phase II in humans. In the meantime, we can begin to look at clinical efficacy with remaining drug already in existence in naturally infected dogs with Valley Fever.

For this study, ten to twelve 5-15 kg (11-33 lbs) dogs with Valley Fever will be enrolled to receive Nikkomycin Z for 60 days. The reason for the size constraints on the dogs is that we only have 250-mg capsules to work with, and we do not have enough to enroll bigger dogs. This optimizes our use of the limited supply of medication. The dogs to be enrolled must have confirmed Valley Fever illness by more than one method, e.g., x-rays and a blood test that are consistent with Valley Fever diagnosis, or positive Valley Fever test with changes on the blood counts and blood proteins that are consistent with Valley Fever. Or the dogs can be diagnosed by visualizing the fungus in tissues or fluids and this is definitive for infection regardless of the results of other tests.

Dogs that are enrolled will receive 1 capsule of Nikkomycin Z twice daily for 60 consecutive days. Between days 21-30 of treatment, dogs will be hospitalized for one day, a jugular vein catheter will be placed, and 6 blood samples will be collected from the catheter during the ensuing 12 hours. This is to study the rate at which the dog absorbs and eliminates the drug. The reason for placing the catheter is to prevent the dog from having the vein punctured several times in one day, which is both painful to the dog and can damage the vein. At the end of 60 days, the dog will come in for an exit examination. At the exit examination, the dog will get re-x-rayed and get all the blood work repeated, including the Valley Fever test, as well as physical examination and determining how the patient is doing clinically from the perspective of the owner.