

Funded Study: Itraconazole Drug Monitoring in Dogs with Blastomycosis

Study Title: Improving Treatment of Canine Blastomycosis with Therapeutic Drug Monitoring

Purpose of Study/Background/Objectives:

Itraconazole is an antifungal drug and is the drug of choice for treating blastomycosis in dogs. Although it is generally effective, blood levels of itraconazole vary significantly from dog to dog. If drug levels are too low, then the infection may not be cleared and, if drug levels are too high, serious side effects can occur. One way to overcome this problem is therapeutic drug monitoring, which means measuring drug blood levels and adjusting the drug dose to achieve ideal blood concentrations. Therapeutic drug monitoring is available for itraconazole in dogs. However, it is not used consistently because we don't know how frequently it should be performed. Therefore, the purpose of this study is to establish a protocol for itraconazole therapeutic drug monitoring in dogs.

Inclusion Criteria:

- At least 6 months of age
- Diagnosis of blastomycosis (see eligibility diagnostics)
- Clinically stable (e.g., not in respiratory distress, not rapidly progressive)
- If antifungal therapy has been started, must be on it for LESS THAN 2 weeks.
- If anti-inflammatory therapy has been started (NSAIDs or pred \leq 1 mg/kg/day), must be on it for LESS THAN 2 weeks.
- NOT on drugs known to alter liver metabolism (e.g., phenobarbital), itraconazole absorption (e.g., antacids), immune response (e.g., cyclosporine, chemotherapy).
- NO evidence of liver disease.
- NO concurrent systemic illness. Dogs with non-systemic illness (e.g., osteoarthritis) may be eligible.

Eligibility Diagnostics:

Prior to consideration for study admission, the patient must have a diagnosis of blastomycosis defined as (1) a positive *Blastomyces* urine antigen test, cytology, histology, or culture AND (2) clinically detectable disease attributable to blastomycosis (e.g., lung or bone lesions on x-rays, skin lesions, uveitis/retinitis, enlarged lymph nodes). The patient must also have a bloodwork demonstrating adequate liver function. Pet owners are responsible for the cost of diagnostics needed to meet these criteria (performed by the primary veterinarian or at the veterinary teaching hospital). These results will be reviewed by study staff before scheduling the study admission consultation and visit.

Treatment/Protocol:

At the admission visit, the patient will be prescribed itraconazole at a standard dose. Every two weeks, serum itraconazole levels will be checked and the dose adjusted. Once the drug levels are in the target range, rechecks will be monthly. Response to therapy will be assessed periodically with relevant diagnostics (e.g., eye exams for patients with uveitis/retinitis; chest x-rays for patients with lung lesions) and the *Blastomyces* urine antigen test. Bloodwork will also be performed to monitor for toxicity. Once clinical signs resolved and diagnostics indicate possible remission, itraconazole therapy will be stopped and a final recheck exam performed one month later.

Owner Commitments:

- Reliably attend visits at the U of I Veterinary Teaching Hospital every other week to monthly for up to 1 year.
- Administer itraconazole capsules to the patient daily (ideally at dinnertime with food) and record administration on a provided form.
- Cover the cost of all diagnostics and treatments not covered by the study. This includes costs associated with potential side effects of itraconazole.
- Communicate regularly with study staff and notify them of any concerns regarding the patient or study participation.

Compensation:

Once enrolled, the study will provide itraconazole for the patient at no cost during their participation for up to 1 year. Study visits and monthly blood and urine testing will be covered. The cost of eye exams will also be covered for patients that require them. Please note, these benefits can only be provided if performed at the U of I Veterinary Teaching Hospital. The cost of other diagnostic tests (e.g., x-rays, cytology) and therapies (e.g., drugs, hospitalization, surgery) are the financial responsibility of the owner.

Contact Information:

If you believe your patient or pet may be a candidate for this study or have any questions, please contact Dr. Jennifer Reinhart at jreinha2@illinois.edu.

