MULTI-OMIC FELINE HYPERTROPHIC CARDIOMYOPATHY STUDY IN LABORATORY CATS

TriviumVet recently completed a pilot study to characterize multi-omic, histopathologic, and gross effects of intermittent dosing with TRIV202. The study examined tissue-, urine-, and plasma-level proteomic and tissue-level transcriptomic effects of intermittent ultra-low-dose and low-dose TRIV202 once weekly. This study was conducted in six cats from a feline research colony with naturally occurring, hereditary HCM. Control HCM tissues were provided from the research colony archives.

Cats that passed screening were randomized to one of the two dosing groups (ultra-low dose and low dose) in a 1:1 ratio and received TRIV202 once weekly for 8 weeks. The primary data and sample collection study days of the in-life phase were at Screening (within 10 days of Day 0) and Day 56. Sampling on these days included blood and urine collection for proteomic analysis. Additional data collected on these days included a physical exam, systolic blood pressure, an echocardiogram and electrocardiogram, a comprehensive biochemistry panel, a complete blood cell count, high sensitivity troponin, NTproBNP, and urinalysis. On Day 60, humane euthanasia occurred and tissue collection was performed. TRIV202 was well tolerated in cats receiving both doses for 8 weeks.

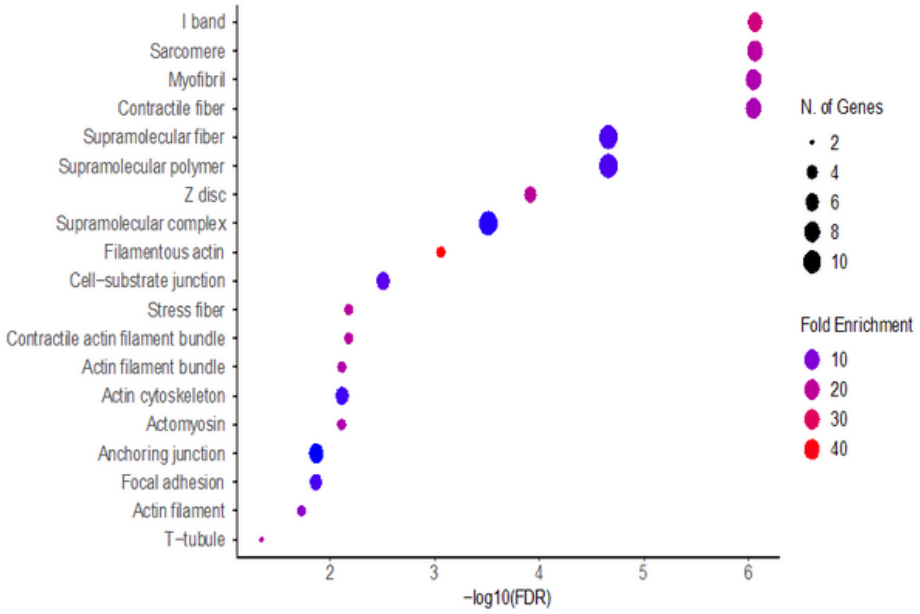

FIGURE 2 GENE ONTOLOGY CELLULAR COMPONENT FOR LEFT VENTRICLE TISSUE; UPREGULATED DIFFERENTIALLY EXPRESSED GENES COMPARING ULTRA-LOW- VS LOW-DOSE CATS

Following repeated weekly dosing, transcriptomic differences between the ultra-low- and low-dose groups highlighted dose-responsive suppressive effects on myocardial hypertrophy and stimulatory effects on autophagy. Differences in the myocardial proteome between treated and control cats suggest potential anti-coagulant/-thrombotic, cellular remodelling, and metabolic effects of the drug. The results of this study indicate potential modes of action of TRIV202 as a HCM disease-modifying agent. Further research is warranted into the relationship between TRIV202 treatment and the most compelling gene expression and protein abundance differences reported.