



WINN FELINE FOUNDATION

For the Health and Well-being of All Cats

637 Wyckoff Ave., Suite 336, Wyckoff, NJ 07481 • www.winnfelinefoundation.org
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TARGETED THERAPY FOR FELINE PULMONARY CARCINOMA

PROJECT STUDY: Targeted therapy for feline pulmonary carcinoma through exploitation of preferential NQO1 expressions and the drug isobutyl-deoxyxyboquinone (IB-DNQ).

Principal Investigators: Alycen P. Lundberg, Timothy M. Fan, Paul J. Hergenrother, Anne, M. Barger;
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Interim progress report summary, W18-021

Treatment available for cats with primary pulmonary carcinoma is very limited, and the outcome is very poor for most of them as they often present with very advanced stages of disease that are not amenable to surgical excision. Because of this, new treatments are desperately needed.

The investigators have been working with a novel anti-cancer agent called isobutyl-deoxyxyboquinone (IB-DNQ) that causes cell death by generating reactive oxygen species in tissues with high levels of NQO1 protein while sparing normal tissue. They have had success with this compound in cats with oral squamous cell carcinoma, and now have the opportunity to explore its potential as a superior therapeutic for cats with pulmonary carcinoma. Importantly, the cat can serve as a comparative model for humans with non-small cell lung carcinoma.

Their main objective of this clinical trial was to evaluate nine total cats in a single-arm, prospective clinical trial to determine if this compound is safely tolerated in cats with pulmonary carcinoma and if the compound exerts anti-cancer effects in patients suffering from this cancer. For the first 12 months of the trial, they had very few inquiries from the referring veterinary population regarding this trial and had difficulty obtaining patients. The reasons for this are that it is an uncommon cancer in cats, and often times their disease is too progressed by the time it has been discovered. Additionally, they needed to create more visibility for the trial. They enhanced the visibility of the trial by using social media accounts to advertise it, increased the postings on the College of Veterinary Medicine's website, and had articles published in the local newspaper. This alone increased the number of veterinarians and pet owners who reached out to them seeking help for cats with this cancer, and they had greater than 15 inquiries and pet owners interested, and ultimately enrolled five patients total. Unfortunately, what they found is that a majority of patients were very late in their stage of disease at the time of diagnosis and were not stable enough to make it to the investigators for project enrollment; therefore, despite having interest, they were unable to treat many cats.

Of the five cats they enrolled, four completed the trial. One patient achieved a partial remission, three achieved stable disease and one had progressive disease for an overall biologic response of 80%. All of these patients have experienced mild, and transient clinical signs with administering of the treatment (hypersalivation, tachypnea, defecation) and all have resolved when treatment stops. None had any significant blood work changes that would indicate any toxicity associated with treatment.

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The investigators are waiting to run the urine 8-OHdG for oxidative damage as their campus has been closed to research activities following COVID-19 stay at home orders.

For determining their second main goal, the investigators are evaluating the response of the tumor to therapy and seeing if there is a correlation with the amount of protein present in the tumor cells and the tumor's response to IB-DNQ. The previous studies have shown that higher levels of NQO1 protein in tumors will result in increase in cell death when exposed to cytotoxic levels of IB-DNQ. Each patient that enters the trial will need to have cytology saved from the tumor that they can stain with IB-DNQ antibody and score a protein level. They predict that higher levels of NQO1 protein in cancer cells will have a better response to therapy. Of the five patients enrolled, the investigators had three samples that were usable and were able to demonstrate moderate to high levels of NQO1 protein in these.

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