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## Getting a Grip on Bone Cancer

Clinical trial tests new treatment drug

By Heidi Jeter

“Osteosarcoma.” Greyhound lovers are all too familiar with this dreaded word. For yet unknown reasons, this beloved breed is highly susceptible to bone cancer. Unfortunately, treatment options haven’t changed much in the past 20 years. The good news, though, is that new therapies lie on the horizon. In a current clinical trial, scientists are evaluating an already available drug to determine its effectiveness in helping dogs diagnosed with bone cancer, including greyhounds.

The clinical trial is part of Morris Animal Foundation’s (MAF) recently launched Canine Cancer Campaign, whose goal is to cure canine cancer within a dog’s lifetime – the next 10 to 20 years. World-renown scientists will work together on MAF-funded research projects that will lead to breakthroughs in prevention and treatment for dogs with cancer.

“One in four dogs will die of cancer and half of all dogs will suffer from it,” says Dr. Patricia N. Olson, president/CEO of MAF. “This clinical trial is part of a large-scale effort to encourage collaboration on a national level to address this serious health problem.”

The organization hopes to raise \$30 million toward these efforts. One piece of the campaign is a bone cancer clinical trial led by the National Cancer Institute (NCI), Center for Cancer Research – Comparative Oncology Program, along with four universities with veterinary colleges who are members of NCI’s Comparative Oncology Trials Consortium. While NCI hopes to discover new treatments for humans with bone cancer, particularly children, MAF and the veterinary schools are focused on helping dogs. It’s a true win-win situation for both species.

“The results of this trial will be as valuable to pet dogs as it is to humans,” says veterinary oncologist Dr. Chand Khanna, director of NCI’s Comparative Oncology Program. “It’s a unique situation. There is a true balance between the dog patient and the human patient in terms of goals.”

## Moving Treatment Forward

Khanna started his career in veterinary oncology about 20 years ago, and he says not much has changed to improve treatments or increase survival rates. Many greyhound lovers are familiar with today’s gold standard for treatment – surgical amputation of the leg with the bone cancer tumor. That treatment is the same one that was used two decades ago. It’s a good option. Dogs heal well and easily adjust to moving

about on only three legs. Often amputation is followed by chemotherapy, which improves the outcome for dogs but doesn't ensure long-term survival.

The problem, Khanna explains, is that even after amputation, microscopic cancer cells remain in the dog's body and eventually spread. About 90 percent of dogs who have surgery to remove the tumor have a recurrence of cancer in the lungs within one year of treatment. The one-year survival rate for dogs who undergo amputation and chemotherapy is about 50 percent, with only about 20 percent of dogs surviving longer.

"The reason dogs die from osteosarcoma is because we can't do enough to stop the spread after surgery," Khanna says. "We realized that we need to do more for dogs after the tumor is managed with surgery."

Dr. Cheryl London, a cancer researcher at Ohio State University, agrees. Her lab, which is participating in the trial, has done extensive research on bone cancer as well as other cancers that affect dogs. She says amputation is great for eliminating the tumor and chemotherapy can delay the cancer's recurrence, but it almost never cures the patient. That's why new approaches to the disease are so important.

"For all types of cancer, it's really important to look at novel therapeutics," London says. "We've hit the wall in our ability to treat cancers with chemotherapy and radiation because these treatments don't fully stop the disease's spread."

The answer to improving long-term survival may lie in a drug called rapamycin. This drug is already used successfully as an immunosuppressive agent in people who have undergone organ or bone marrow transplants. Recent research at NCI and elsewhere has indicated that it may also block an important pathway in cancers, the mTOR pathway. This pathway allows cancer cells to sense their nutritional status and thus, improves their ability to grow and spread. A number of drugs similar to rapamycin are being developed that may inhibit the mTOR pathway.

This type of targeted therapeutic approach has been fairly successful in treating some human cancers, London says. First, however, researchers must identify that there is a target. Then they must determine if there is a drug available that can safely inhibit that target. In the case of rapamycin, the researchers must determine whether the dose that is effective in dogs will be safe and won't cause major side effects.

The first stage of the MAF-funded clinical trial, which began earlier this year, looks at whether the drug is safe and then what the appropriate dose would be to inhibit the cancer.

### **Completing phase one of the clinical trial**

About 25 dogs will be enrolled in phase one of the study, all of them diagnosed with bone cancer and awaiting treatment. Each participating dog underwent a simple tumor biopsy and then received rapamycin prior to surgery. After the tumor was

removed, researchers compared it to the biopsy to determine whether the mTOR pathway was turned off. If it was, that would indicate the drug has the potential to be effective as a treatment.

Four universities are participating, including the Ohio State University, the University of Illinois, the University of Wisconsin and Colorado State University.

"We're very fortunate that Dr. Khanna invited us to be part of this study," says Dr. Tim Fan, lead researcher on the team at the University of Illinois.

Fan and his scientific team have conducted extensive work on managing pain in bone cancer patients. Through a current study funded by MAF, his team is evaluating the use of a drug called pamidronate, which he hopes will decrease pain and increase quality of life for dogs with osteosarcoma. Many of his patients in this study are greyhounds and rottweilers, and his team is dedicated to helping these dogs. He emphasizes how important clinical trials are in this mission.

"We want to find new treatments for osteosarcoma, and we can't do that without pet owners who are willing to help us investigate this disease process," Fan says.

The benefits to dog owners whose pets participate in the rapamycin trial include the evaluation of a potentially safe and effective drug for treating osteosarcoma, and the offsetting of costs associated with conventional treatment options. This can be of great help to pet owners who want to give their dogs the best treatment possible. Oftentimes, a pet may have a treatable health concern, but the owner doesn't have the financial means to treat the animal. For example, Fan says about 75 percent of the pet owners participating in an ongoing bone cancer pain study at the University of Illinois would not be able to afford to treat their dogs at all if they weren't enrolled in the study.

"With these clinical trials, we can investigate and provide cutting-edge therapy to patients that they may not get otherwise," Fan says. "MAF-funded studies such as these serve as a wonderful avenue to allow pet owners to pursue conventional therapies for their pets and to allow researchers to evaluate novel therapies at the same time."

### **Next steps**

If this novel treatment works, phase two of the trial will seek to determine whether the drug combined with chemotherapy can treat dogs whose cancers have already spread. Khanna cautions that even if rapamycin is very effective, which they hope to determine by the end of this year, it will probably take five years or so before it would become standard treatment. Still, this clinical trial is a good first step and if things progress as hoped, dog owners will have a great treatment option for their sick dogs.

“Rapamycin is a generic drug so it’s available already and it could be relatively inexpensive,” Khanna says. “If it works, it would be a simple way for pet owners to improve treatment of their dogs at lower cost.”

Collaborative research such as that taking place through this clinical trial could help advance veterinary medicine at a much faster pace than before. Multi-center trials have become commonplace in human medical research, but London says, they are just beginning to increase on the veterinary side. The biggest plus side to engaging multiple institutions is that it is easier to enroll the number of necessary patients and usually results are seen faster. As Fan says, individuals can be successful in their fields of research, but by pooling the talent together, even bigger breakthroughs can be made. Khanna agrees, saying that this type of collaboration, involving human oncologists and veterinary specialists, is necessary to improving the health of all species.

“There’s a lot of interest and enthusiasm for this study,” Khanna says. “It’s an example of how people with common and overlapping interests can do a lot more together than they would by themselves.”

That’s good news for humans, dogs and other species as well.

*To learn more about MAF’s Canine Cancer Campaign, go to [www.curecaninecancer.org](http://www.curecaninecancer.org).*