

Pet Dogs Help Test Cancer Vaccine

By Susan Chaney

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A dozen or so dogs will be part of the first test of whether a vaccine may eventually be used to treat osteosarcoma, a cancer which ultimately kills almost all dogs treated for it.

Right now, six dogs with osteosarcoma have been vaccinated at the [University of Pennsylvania's School of Veterinary Medicine](#). All dogs have undergone limb amputation to remove the primary tumor and follow-up chemotherapy prior to receiving the vaccine. Another four dogs will likely be vaccinated this month, and lead researcher Nicola Mason, B.V.M., Ph.D., and her team are already screening dogs for the next phase.



Five-year-old Bulldog Erma is part of a trial to determine whether a cancer vaccine is safe. Nicola Mason, B.V.M., of the University of Pennsylvania's School of Veterinary Medicine is leading the trial. Photos courtesy of University of Pennsylvania.

The vaccine consists of a genetically modified form of the bacteria listeria. It is modified to be much less virulent and to carry a tumor protein, Her2/neu. Phase 1 of the trial is testing the safety of the listeria vaccine which prompts a dog's immune system to attack both the bacteria and the tumor protein it carries, thus generating an immune response against cancer cells. "The immune cells are geared to attack listeria, but they will also be trained to recognize and attack cancer cells that express the Her2/neu protein," Mason says. "This protein is one of the few markers that distinguish cancer cells from healthy ones, so the stimulated immune system should attack the cancer.

"The vaccine aims to train the body's immune system to attack cells that express the Her2/neu protein. We know that 90 to 95 percent of dogs with OSA have cancer cells somewhere else in their body at the time of diagnosis because despite limb amputation and follow-up chemotherapy they still die of their disease. The vaccine aims to stimulate an immune response that will target and kill these remaining tumor cells and so prevent recurrence of the tumor."

About 50 percent of dogs with osteosarcoma express the Her2/neu protein in their tumor, Mason says. "Human tumors that express Her2/neu tend to be more aggressive than those that do not express Her2/neu. Patients with these Her2/neu positive tumors tend to have poor prognoses," she explains. "Our preliminary data suggest that the same is true in dogs, that is, dogs with Her/2-expressing OSA tend to have more aggressive disease." This has not been confirmed yet, but the suggestion of that possibility, she says, comes from data that's been published and the data her team is collecting during the trial.



Sasha was the first dog to be vaccinated with modified listeria, designed to educate the dog's immune system to attack the listeria as well as cancer cells.

Although Phase 1 is about primarily about safety, the team is also looking at its therapeutic benefit. Two dogs in the trial have lived beyond the one year that most dogs survive after osteosarcoma treatment. One dog died before the first year passed. "The other three dogs are still alive and tumor-free, but haven't quite made it to a year yet," she says.

"Probably by the end of the summer we'll have a good feel for whether we're making a difference in the long term survival of these dogs."

The team has seen very few side effects. "So far, it's been very safe, both in acute and long-term follow-up," Mason says. "At the doses we've tried thus far, it's safe. That's really what we're interested in currently and that is very important."

One missing piece of information is the median survival of dogs that express the Her2/neu protein. It may be that the dogs in the study would have died before that one-year mark without the listeria vaccine, or perhaps they would have lived longer than a year even without it.

A collaborator of Mason's, Yvonne Paterson, Ph.D., a professor of microbiology at the University of Pennsylvania, has worked with modified listeria for much of her career. She knew it was a very strong stimulator of the immune system and recognized its potential to stimulate anti-tumor immune responses. "The idea is to genetically modify the bacteria so that it carries a little bit of tumor with it – the Her2/neu molecule. Then, when it is introduced into the body it will stimulate an immune response against cells that express Her2/neu. We are using the listeria as a Trojan horse," Mason says.

Phase 2 of the trial will evaluate the effectiveness of the vaccine. "People who have dogs with osteosarcoma and are interested in participating in the clinical trial are welcome to contact me" through the [university website](#), she says.

The listeria vaccination strategy, which is also being evaluated in women with cervical cancer, is being used by Advaxis, and Mason indicates that the Phase 2 clinical trial with the vaccine will be funded. "We're interested in developing an effective vaccine for dogs," Mason says. "Advaxis has a strong interest in making the vaccine available for veterinarians to use. However, if we find that this vaccine is effective in dogs with spontaneous tumors, then the chances are it will also work in humans.

“I really feel that we can help the dogs, and, as a bonus, we may be able to help humans as well. That just makes a lot sense.”

Mason is also looking for funding to evaluate the effects of the vaccine on dogs that have not had a leg amputated. These would be dogs that may have severe arthritis, problems with their cruciate ligaments or are just too big to move around well without a front leg. “We are interested in combining the vaccine with palliative radiation.” The study would determine whether an immune response along with radiation could kill the tumor. “We have the protocol set,” Mason says. “We’re waiting for institutional approval and looking for funding.”

The assistant professor of pathobiology and clinical studies is clearly upbeat by the promise that listeria holds. “It’s very exciting,” she says.

All of the dogs in Phase 1 have been examined, tested and vaccinated at the University of Pennsylvania. Nonetheless, the six enrolled dogs are from Ohio, North Carolina, Massachusetts, Delaware, New Jersey and Pennsylvania. The dogs are scheduled to be vaccinated next are from Illinois and Florida. The dogs needed to be close enough to travel to Philadelphia for checkups and in the case of some negative side effect. For Phase 2, Mason says it’s likely a couple of other academic centers will be involved. If so, dogs in those areas will also be able to participate.

Dogs in Phase 1 receive three listeria vaccinations three weeks apart, after which the dogs remain in the veterinary teaching hospital for 24 to 48 hours to monitor for any adverse reactions. In the next phase, dogs will also receive a single booster vaccine every two to three months to maintain immunity against the tumor. This vaccination schedule will be continued until such time as the disease progresses.

“Right now, things are starting to look quite promising,” Mason says.

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