

ALLIANCE FOR CANCER GENE THERAPY'S MIRACLE IN THE GENES:

A GOLDEN RETRIEVER'S TALE

I am a Cancer Gene Therapy Poster Dog! My name is Barney, I am a 13-year-old Golden Retriever and I live just outside Philadelphia. I am lucky to have as loving owners Carol and Barry Doohan. At age six, with half my life ahead of me, complete with a loving family and a huge backyard, life was very good. The only time I had ever been sick was with Lyme Disease, which is not uncommon in Central Pennsylvania. Then came what was to become an eventful trip to the vet for a final and routine Lyme check-up. Ushered into the familiar back of the family Jeep I was off on a journey that would not only change my life but perhaps that of many other dogs and perhaps some people. I had been to see Dr. Lauren Strine at Longwood Veterinary Clinic many times before. On this visit, my owner's body language told me that something was very different. Dogs understand body language better than words!

DOGS ARE ASYMPTOMATIC

I heard the conversation all right, but advanced "Stage Four Lymphoma" were words not in my daily routine. During a routine physical, Dr. Strine's trained hands found many peculiar lumps. Oddly enough, I felt great! I heard her tell my owner that dogs tend to mask their symptoms. Luckily, she did not take my apparent well-being for granted. Suddenly my daily routine changed dramatically.

Dr. Strine placed her hand softly on my shoulder as she always does before something else is about to happen. I heard her say "clinical trials". I wondered, is that anything like field trials for hunting dogs like me? I would soon learn that clinical trials, at which I became very accomplished, were to become much more important to me than retrieving!

I am a lucky dog because Dr. Strine worked in close concert with the University of Pennsylvania's School of Veterinary Medicine and the Matthew J. Ryan Veterinary Hospital. It was located close by my home and it was not

long before I had made so many trips there I could have found my own way! Dr. Strine introduced me to Dr. Karin Sorenmo at Penn Vet. I felt like a celebrity! Dr. Sorenmo is not only an excellent vet, but she is also associate professor of oncology at the University of Pennsylvania's School of Veterinary Medicine. When you are a sick dog, this is where you want to be.

Now, the story gets more complicated. As it turned out it is a good thing that Dr. Strine did not start chemotherapy for my lymphoma back at Longwood when she first found the lumps because if she had, I would not have been eligible to be treated in a clinical trial at U Penn Vet specifically designed for advanced lymphoma in dogs.

Penn Vet. is located next to the Perelman School of Medicine at the University of Pennsylvania where coincidentally associate professor of hematology and oncology Dr. Robert H. Vonderheide has his laboratory. Dr. Vonderheide's investigative research into cancer gene therapy and immunology was initially funded by



a grant from the Alliance for Cancer Gene Therapy of Stamford, Connecticut.

Little did I know that because many good folks loved me, I was about to be among the very first dogs in the world treated with a new cancer gene therapy for non-Hodgkin's Lymphoma. It was a little frightening because the doctors told my owners there were no guarantees of success in clinical trials.

Dr. Vonderheide together with Dr. Nicola Mason, an assistant professor at Penn Vet., had established a clinical trial to determine whether a genetically engineered vaccine would eliminate the cancer or prolong life for dogs like me with Non-Hodgkin's Lymphoma. I had standard chemotherapy followed by three doses of this vaccine, prepared from my own cells, administered over a nine-week period. No, it did not hurt but you have to lie still for a short time while the specially treated cells are injected into your body. I am told they now hope to use the same vaccine treatment for humans. Here is how it works.

Cells are taken from my blood (takes a long time), treated with material from my tumor and then infused back into my body. These new cells stimulate my immune system to attack and kill the cancer cells. Guess what, I did not have any side effects except that on each trip my faced itched on the way home in the car! All dogs scratch anyway.

I turned thirteen this August and aside for a couple of scrapes and a mole on my lip (non-cancerous) I am proud to report that I am in perfect shape! How can I thank everyone involved in saving my life? The answer is to tell folks do not ever be afraid of a clinical trial, because that is what kept this dog in the hunt.

By the way, other dogs have shared my good fortune at U Penn Vet. Dr. Sorenmo has told me about Eljer, a Labrador retriever, enrolled in the therapy in 2008, who never relapsed. Basil is also a Labrador, he is one of the dogs that relapsed relatively quickly after the vaccine, but then went into a durable remission with rescue chemotherapy and has been off chemotherapy for several years!



A Thankful Barney frolics in the Delaware Bay.



There are also several others dogs that lived long and normal lives but died from other causes. Their owners remain very grateful for the opportunity to have had their dog participate in the trial and remain with the families for years. Of course, we cannot forget about Kyra the pioneering gene therapy K-9 success story in 2006, who lived to the age of eleven and died of natural causes.

CLINICAL TRIALS FOR PRIVATELY OWNED ANIMALS *Many Species - One Medicine*

The scientists behind Barney's incredible story are Alliance for Cancer Gene Therapy Research Fellow Dr. Robert Vonderheide of U Penn's Perelman School of Medicine and Abramson Cancer Center along with U Penn's School of Veterinary Medicine's Dr. Karin U. Sorenmo and Dr. Nicola Mason of U Penn Veterinary School.

Says Dr. Vonderheide, "The University of Pennsylvania School Of Veterinary Medicine is intricately involved with the global bio-medical research effort, particularly in the field of gene therapy immunology. I think there is a great opportunity of working together to develop new treatments for cancer because in dogs we have an out bred animal exposed to the same diseases and environmental conditions as humans. The ethics of treating diseases in privately owned animals with informed consent and long-term commitment allow us to test therapies much sooner in the course of the disease than we could test the same therapies in human patients. It is very important to note that we are not talking about using experimental dogs in

these trials. The dog's families bring the animals to us. There have been minimal side effects in the dogs from cancer gene therapy.

"In collaboration with the U Penn Veterinary School, we realized that lymphoma in dogs looked very much the same as human lymphoma. The ability to treat privately owned pets with gene therapy in clinical trials can expedite by a number of years the time line for clinical trials for human patients. There is a two-fold benefit, we can treat the family pet and prepare for human trials.

They have a great motto at the U Penn Veterinary School: *Many Species, and One Medicine*. "That reference describes our unique partnership at Penn Vet," says Vonderheide.

ALL PATIENTS DO BETTER IN CLINICAL TRIALS *"Barney Is Family"*

Dr. Vonderheide is an enthusiastic advocate of cancer patient participation in clinical trials, whether human or K-9. "It is very clear that even for a therapy that is ultimately not-beneficial, there is extensive broader care provided to patients enrolled in clinical trials. Research shows that overall; patients in clinical trials tend to do much better. The care and intense follow-up in clinical trials is extraordinary. It was remarkable at Penn Vet. to see the relationships between the doctors and the dog owners who brought their pets for clinical trial treatment." Says Dr. Sorenmo, "Barney was and is a member of the family!"

LONG TERM K-9 CANCER SURVIVORS

Dr. Sorenmo personally oversaw Barney's treatments. "Several of the dogs from the initial 2007 clinical trials are now long-term cancer survivors and free of disease for more than a year. Overall, these clinical and immunological results suggest that cell-based cancer vaccination is safe and synergizes with chemotherapy to improve clinical outcome in canine lymphoma. More broadly, our findings underscore the unique value of clinical investigations. Thirty privately owned dogs were enrolled in the trial. Nineteen of these dogs were eligible to receive the cancer gene therapy vaccination. Fourteen of those dogs relapsed but were then treated with chemotherapy and did not relapse again, lived extended lives and died of natural causes. Three of the aforementioned dogs remain alive with no evidence of lymphoma. Forty percent of the dogs in the original trials were long-term survivors. Barney, who remains cancer free, was dog number 9 in this trial. His legacy at age thirteen may well transfer to human treatments. We hope to begin human trials with this therapy in three years."

HUMAN CLINICAL TRIAL CRISIS *Sadly, A Lack of Patients*

Vonderheide: "Most major cancer centers in the United States only place 30% of their patients in clinical trials. Pediatric Cancer Centers are a dramatic exception. At pediatric cancer centers, nearly all child patients are placed in clinical trials. The successes of these trials, which have literally cured childhood leukemia, have everything to do with the fact that nearly all children with Leukemia are treated in clinical trials. It is proof of their efficacy and importance."

CHEMOTHERAPY AND GENE THERAPY A SURPRISING AND FORMIDABLE PARTNERSHIP *Knowledge Transfer from Barney and Friends to Humans*

"There is a huge amount of research coming out of immunology labs suggesting the interplay between chemotherapy and gene therapy, says Vonderheide. "On the one hand, chemotherapy can sensitize patients to immune therapy and on the other hand, immune therapies sensitize patients to the good effects of chemotherapy. A much-unexpected result. No one likes the side effects of chemotherapy but we learn more as we move forward toward successful cancer treatment.

Vonderheide: "The big effort in cancer therapy is recognizing that an individual scientist can only do so much but when we team together and pool research and ideas that is where we see the big hits. The work with the dogs



Carol and Barney celebrating a joyous recovery.

really opened our eyes into the power of combining chemotherapy with immunotherapy and this has opened a new avenue of exploration in human cancer treatment. The work with Barney and other dogs with cell-based gene therapy at Penn Vet. has brought us to a tipping point where we can now talk about the real results. It is really happening and the results are stunning! We must all roll up our sleeves and continue to work together."

From Barney, if dogs could speak, comes a wonderful simplification of a complicated, complex and expensive process. "Using the seven year dog to people multiple I am now 91 and still playing Frisbee! What's cancer? I feel great! Doctors Sorenmo, Mason and Vonderheide heartily agree!

ALLIANCE FOR CANCER GENE THERAPY

The Alliance for Cancer Gene Therapy (ACGT) is unique in that it is the only national non-profit organization committed exclusively to cancer gene therapy research that encompasses all types of cancer. One hundred percent of all funds raised by ACGT go directly to support medical research, and since inception in 2001, ACGT has issued close to \$20 million in substantial research grants to 31 researchers through its Investigator Grants for Innovative Gene Therapy Research. ACGT believes that cancer gene therapy has the greatest potential not only to improve the quality of life of cancer patients, but also to ultimately realize a cure for cancer. To learn more, visit www.acgtfoundation.org. □

ACGT will celebrate its tenth anniversary and honor its co-founder the late Edward Netter of Greenwich on Thursday, April 19, at the Hyatt Regency in Greenwich, Connecticut. The Keynote speaker will be by *NBC Nightly News* with Brian Williams Chief Scientific Correspondent Robert Bazell. For further information visit www.acgtfoundation.org or telephone 203-358-8000 extension 705.