

JAY SMITH: I'm Jay Smith, Professor of Physical Medicine and Rehabilitation at the Mayo Clinic in Rochester, Minnesota. I'm the primary investigator on this clinical trial with respect to the use of adipose derived stem cells for the treatment of knee osteoarthritis. Why study osteoarthritis?

Osteoarthritis is the most common joint disease worldwide. And in America, there are nearly 30 million people affected with osteoarthritis, the knee being the most common joint. And the costs of treating and managing osteoarthritis are over \$100 billion a year in this country.

At this point in time, most of our treatments are simply palliative, meaning they control symptoms, they don't really cure the arthritis. Ultimately if the arthritis gets bad enough, there is a total knee replacement. So we, like many other scientists and clinicians, are trying to look for interventions that will actually alter the course of arthritis or prevent it. And stem cells are attractive in that regard.

The primary goal of our current research is to study the safety of adipose derived mesenchymal stromal cells, or stem cells in the treatment of knee osteoarthritis. How this relates to previous research is that there has been a fair bit of basic science and translational research on the potential benefits of stem cells in the treatment of osteoarthritis. We've also performed animal studies in rabbits demonstrating the safety of these cells in the treatment of osteoarthritis in rabbits. And now we're extending that to human clinical trials.

Adipose derived stem cells have received increasing attention for several reasons. First of all, adipose derived stem cells are very prevalent. Stem cells exist all through the body. But there are two areas where stem cells are particularly prevalent, in the bone marrow and in fat.

And actually we have more stem cells in fat than we do in our bone marrow. So extracting stem cells from fat is very attractive in terms of numbers. Stem cells from fat also grow faster and are generally more resilient when you grow them in the laboratory, which makes them very attractive for growing in the laboratory and then subsequently injecting back into patients.

In terms of animal studies for osteoarthritis, there have been many animal studies throughout the world in animals ranging from mice to horses and camels. Our particular research has been using rabbits as a large animal model. And we studied the safety of these particular cells that we'll be using in humans in rabbits.

First, we had to inject the knees of rabbits that were normal to demonstrate that there wasn't any adverse effect of the cells on the knee, and the rabbit that didn't have any preexisting problem. With then did a second study in which we surgically altered the knee of the rabbit to predispose it to osteoarthritis. And so these were rabbits that were at risk for developing early osteoarthritis. And we tested the cells in those knees as well, demonstrating that the cells did not have any adverse effect. And that really paved the way for the human clinical trial.

So we are going to study 20 individuals with knee osteoarthritis. And these individuals will otherwise be healthy. And we're going to be injecting adipose derived stem cells into their knee. Adipose derived stem cells will come from a small piece of fat that's going to be extracted from their abdomen. We'll get the stem cells from that piece of fat, grow them in the laboratory to millions, and then subsequently inject them into the knee.

We have four different groups of people in this study design. And that allows us to give each group of four individuals a separate dose. So each individual will be getting anywhere from 50 to 300 million stem cells into their knee over a one to three month period.

The unique aspects of this particular study is that it will be the first study of its kind to be done in the United States, in terms of using culture expanded adipose derived stem cells. It will be the first study in the world to use multiple doses of stem cells in certain individuals. So this is very important preliminary findings to help us pave the way for future clinical design studies.

So the status of our project at this point in time is as a clinical trial that is utilizing culture expanded stem cells, the FDA considers that a drug. And so we are-- through the FDA, we had to submit an application through the FDA for approval. And we are through the Mayo Clinic IRB.

And so we are ready to enroll patients. We'll probably start enrollment within the next two months. So July, August we'll probably start enrolling our subjects into the study. The enrollment will probably continue for a year and a half. And we'll be following patients up for one to two years after their treatment.

We're going to enroll a total of 20 patients in this investigation. We're going to have four groups of four to five patients depending on recruitment. And each group will get a different dosing regimen. And we'll sequentially and enter them into the protocol.

Clinicians may be wondering which of their patients may qualify for this clinical trial. We're recruiting subjects between the ages of 40 and 70 with knee osteoarthritis that are otherwise healthy individuals.