Research on cancer vaccine begins to pay off

August 20 2010, By Alan Bavley

The vaccine that Larry Mathews is getting won't protect him from the flu. That's OK -- the stakes are far higher than that.

He's hoping the shots will prime his immune system to fight the aggressive cancer that has invaded his brain. If it works as he wants it to, his body's own killer cells will mop up malignant cells that surgery, radiation and chemotherapy couldn't eliminate.

For decades, scientists have been trying to create vaccines like this to recruit the body's immune system to destroy cancer cells the way it wipes out foreign viruses and bacteria.

After many false starts and premature promises, it appears that their research is beginning to pay off.

In late April, the U.S. Food and Drug Administration approved the first cancer vaccine, Provenge, that can modestly extend the lives of men with advanced prostate cancer. Several major insurance plans and Medicare claims processors in some parts of the country, including Kansas and Missouri, already have agreed to pay for the costly treatment.

Mathews is taking part in a preliminary clinical study at St. Luke's Hospital on a brain cancer vaccine developed at the University of Kansas Medical Center. A larger two-year study aimed at gaining FDA approval is planned to start this fall.

Worldwide, scientists are working on dozens of vaccines against

melanoma, breast cancer and cancers of the lung, colon and pancreas.

Researchers can cite anecdotes of cancer patients given months to live who have survived 15 years or longer after receiving vaccines. But so far, conclusive evidence from large clinical trials is scant.

Even so, experts anticipate that several cancer vaccines could prove effective enough to gain FDA approval in the next four or five years.

These therapeutic vaccines are designed for patients who already have cancer. That makes them radically different from conventional preventive vaccines, such as the cervical cancer vaccine Gardasil that immunize against viruses that cause cancer.

The surge in development of therapeutic vaccines doesn't come from any single scientific breakthrough, said William Chambers, director of clinical research and immunology at the American Cancer Society. Rather, it's the result of years of slow, incremental progress.

"Immunotherapy has been a tough nut to crack," Chambers said. "What you're seeing now is the product of a lot of hard work. Some of the successes are showing up."

The immune system identifies alien organisms in the body and then seeks out and destroys them.

But cancer cells generally get a free pass. For one, they're very similar to normal lung or prostate or colon cells. And as they grow, they evolve ways to turn off an immune response or cloak themselves from detection.

The goal for vaccines is to train the immune system to recognize ways that cancer cells differ from normal cells and motivate it to attack.

By trial and error scientists have identified targets on cancer cells, called antigens, that the immune system can identify as different from normal cells. They also better understand components of the immune system that recognize antigens and alert the immune system's killer cells.

Vaccines represent a major shift in thinking about how to treat cancer, said James Gulley, a researcher at the National Cancer Institute. Conventional cancer therapies aim toxic drugs and radiation at tumors, but can harm other tissues and cause nausea, fatigue, hair loss and other side effects.

Vaccines narrowly target the immune system. Side effects -- fever, chills, soreness at the injection site -- typically aren't much greater than what you may get from a flu shot. But getting vaccinated can take much longer than a flu shot.

Consider the TVAX vaccine that Mathews is receiving.

While some cancer vaccines use standard antigens commonly found on tumors, other vaccines like TVAX must be tailor-made from the patient's own cancer cells. A course of TVAX takes about 10 weeks, with plenty of visits to the doctor.

After surgery, the patient's cancerous brain tissue is sent to a lab for processing. Tumor cells are irradiated so that they no longer can multiply. Then the cells are mixed with a drug that stimulates the immune system.

The patient gets an injection of this vaccine and a couple weeks later, a booster shot.

But the process doesn't stop there.

While the patient's immune system comes to recognize the cancer cells as something foreign, it still isn't ready to mount an attack. So the patient's blood is run through a machine that skims out immune cells. These cells are processed to launch an assault on the cancer and then transfused back to the patient.

A couple of weeks later, the whole process is repeated.

TVAX has gone through three versions since immunologist Gary Wood began working on it at the University of Kansas Medical Center two decades ago.

"Every tumor is unique from an immunologic standpoint, so the best responses are generated by the patient's own cancer," Wood said. "It took a while to simplify the manufacturing process to make it more available."

Mathews has been making regular trips to Kansas City from his home in Green Bay, Wis., for TVAX treatments.

"Instead of more chemo and radiation, I'm looking to the vaccine," the 47-year-old hospital administrator said. "It doesn't sound as toxic and debilitating."

For Michael Salacz, the St. Luke's brain cancer specialist conducting the TVAX trial, the vaccine is an alternative for patients who have run through the conventional therapies and may have just a few months to live.

"I don't have a whole lot else in the cupboard to offer these patients," Salacz said. "This is a search for something better, to strike out and offer something new, rather than to offer something with little hope."

Based on results from about 180 patients who've already received one or another version of his vaccine, Wood expects to see patients' survival at least doubling, on average, to about six months. He's optimistic that it may add a year to the lives of some patients.

The study that won FDA approval for Provenge found that it extended survival of patients with late-stage prostate cancer by about four months. That may not seem very long for a vaccine regimen priced at $93,000.

But those results could improve if patients receive vaccines early in treatment, rather than as a last resort, Wood said.

It's a belief shared by Gulley of the National Cancer Institute.

"The basic issue is we have been looking at patients who are too advanced," Gulley said.

Some clinical trials use cancer patients who aren't expected to live long because they can show very quickly if a vaccine will prolong survival.

Another reason advanced patients get vaccines is that cancer specialists are more likely to use standard treatments before trying something experimental.

"This old paradigm may not be the best way to study vaccines," Gulley said.

For vaccines to be effective, a patient's immune system has to be intact, but cancer treatments can "beat up" on it, Gulley said. And tumors that have been around a while can shut down the immune system around them.

Research suggests that the immune system needs time, as long as a year,

to build an adequate response to cancer after getting an initial boost from a vaccine, Gulley said.

As immune cells pick apart a tumor, the immune system may find new ways to attack the tumor on its own. Studies in mice show that given time, vaccines trigger what scientists call an "antigen cascade."

"That's the beauty of the immune system," Gulley said.

Once the immune system is fully activated, it may be able to keep a cancer in check, dramatically slowing the growth of tumors. Cancer would become a chronic disease managed by occasional booster shots, Gulley said.

Whether vaccines will ever provide a complete cure remains to be seen, Gulley said.

But for Wood, that has to be the goal.

"Our bar is set pretty high," he said. "We want (survival) to be more than a few months. We want it to be a lot."

When the immune system fights a cold or flu, "you recover from those diseases completely," Wood said. "From the data I've seen, that's possible with cancer."

And Mathews?

"My hope is it works for me," he said while visiting St. Luke's. "If it doesn't work for me, my hope is we move it along so it works for somebody else."