GENE THERAPY

Questions Remain on Cause of Death in Arthritis Trial

An investigation into the death of a 36-year-old woman in a gene therapy trial has revealed a complex tragedy but reached no firm conclusion on whether the experiment was to blame.

At a meeting this week, the National Institutes of Health’s Recombinant DNA Advisory Committee (RAC) largely discounted a theory that a vector used in the trial multiplied out of control, among other hypotheses. Participants noted that the patient apparently died because she had a severely compromised immune system and succumbed to a fungal infection.

Gene therapy, which has been blamed for two deaths in the past 8 years, did not get charged with a third. Some concern had focused on the popular vector used in this experiment, adeno-associated virus (AAV). Results presented at the meeting did not challenge the consensus that it is relatively safe. However, questions remain about how well the patient was informed and how she was selected for the trial; her disease was not life-threatening. Concluded Arthur Nienhuis, president of the American Society of Gene Therapy: “We see areas in which we need to be concerned.”

The patient, Jolee Mohr of Springfield, Illinois, had suffered from rheumatoid arthritis since she was 21. Through her rheumatologist, she enrolled in a phase I/II safety trial of a new treatment for arthritis sponsored by Targeted Genetics Corp. in Seattle, Washington. The study involved injecting into joints AAV that carried a gene coding for a protein that inhibits a proinflammatory cytokine called tumor necrosis factor α (TNF-α). Mohr received an initial injection in her right knee on 26 February and a second on 2 July.

After the second injection, she developed flulike symptoms. Ten days later, she was admitted to the hospital and was later transported to the University of Chicago Hospital. She died there after massive organ failure on 24 July. The Food and Drug Administration, which reported to the University of Chicago Hospital and was later transferred to the University of Chicago Medical Center. In addition, she had a large abdominal hematoma, or a blood clot.

Tests done after Mohr died show that she already had a mild Histoplasma infection on 2 July. Because she also tested positive for herpes simplex virus, some experts have suggested that herpes proteins, along with wild AAV, could have helped the AAV vector to replicate and weaken her immune system. But although the AAV vector did escape from the injected joint to other tissues, the levels were extremely low, making it unlikely the virus was replicating, RAC found.

A more likely culprit is an immune-suppressing drug she was taking. This drug, called Humira, is a TNF-α blocker like the gene therapy product and has been associated with Histoplasma infections. One possibility is that the combination pushed Mohr over the edge. The RAC members hope an experimental assay can tease apart levels of gene product and drug in Mohr’s blood.

More definitive results should be available by the next RAC meeting in December, said chair Howard Federoff of Georgetown University in Washington, D.C. Meanwhile, however, Federoff and others say other questions remain unanswered—such as whether Mohr realized that patients weren’t expected to benefit from this study.

—JOCELYN KAISER

Taking ADHD to Heart

U.S. academic researchers are teaming up with health insurers to learn whether drugs used to treat hyperactivity also cause heart problems. They will be looking at the health records of 500,000 children and adults who have taken any of a half-dozen drugs for attention deficit hyperactivity disorder (ADHD) in search of higher rates of sudden cardiac death, heart attacks, and stroke. The $4 million study may also provide clues about “how risk changes with age, gender,” and other variables, says Michigan State University’s Marsha Rapley, chair of the pediatric advisory committee at the Food and Drug Administration. FDA is co-funding the study with the federal Agency for Healthcare Research and Quality.

—JENNIFER COUZIN

Space for Rent …

With no money for new biomedical research aboard the international space station, NASA is hoping that a sister agency will open its pocketbook. A new agreement between NASA and the National Institutes of Health is intended to open doors for NIH-funded scientists proposing projects to take advantage of the station’s microgravity environment. “The funding will come if we have competitive, highly meritorious grants,” says cell biologist Danny Riley, president-elect of the American Society for Gravitational and Space Biology. The station is scheduled to open for business in 2011.

—BENJAMIN LESTER

… And Google Air?

Two Gulfstream jets took off recently from NASA Ames Research Center at Moffett Field in California to observe a meteor shower high above the haze of San Francisco Bay. The front-row seats for astronomers came courtesy of a deal between NASA and a private company run by Larry Page and Sergey Brin, founders of the Internet giant Google.

Last month, NASA granted the planes access to Moffett Field, located near Google’s base in Silicon Valley and typically off-limits to private aircraft, in exchange for their use on research missions. The two Gulfstreams and a Boeing 767 will be housed for $1.3 million to $2.3 million a year, says Steven Zorneter, Ames associate director for institutions and research, and outfitted with a suite of atmospheric sensors that will be activated whenever the planes are in the air.

Outside researchers, who are welcome to submit proposals, may be attracted to the king-sized beds on the Boeing jet, whose commercial version carries 180 passengers. —ANDREW LAWLER