Posted on Mon, Dec. 20, 2004

Parkinson's patients denied drug they say really helps

By Karla Ward And Linda Blackford
HERALD-LEADER STAFF WRITERS

His body ravaged by Parkinson's disease, Dan Webster considered himself "just about ready for the nursing home" several years ago.

He had given up his job as a computer programmer and used a wheelchair to get around. Then an experimental drug being tested at the University of Kentucky changed that.

In September 2002, Webster had a pump implanted in his abdomen that delivered a steady dose of a drug -- glial cell line-derived neurotrophic factor, or GDNF -- to the affected area of his brain via tiny catheters.

After a while on GDNF, Webster said, he no longer needed the wheelchair, began looking for work and felt well enough to install water lines to his father-in-law's house last summer.

"I felt so good," he said. "The feeling of malaise went away, went far away."

Now, because of safety concerns, the drug trial has been stopped, and Webster, 57, is gradually relapsing to his previous condition.

The decision to stop the trial leaves Webster, nine other patients at UK, and others around the country facing the prospect of going back to the way they were -- just as many of them felt they were getting better.

The story has received national attention, not just because of the patients' dramatic improvements, but because the situation shows how, in the complicated world of drug development, business can conflict with patients' and even researchers' desires.

A halt, a protest

"After 22 months of constant steady improvement, I have to move slow and slothlike again," Webster said. "My voice comes and goes ... rigidity causes constant pain."

Parkinson's disease is a progressive brain disorder characterized by shaking, slow movement and muscle stiffness.

Unlike other drugs, which alleviate the symptoms, GDNF appeared to slow or even halt the progress of the disease itself, according to the UK study and in a similar study in Britain.

In May, Dr. Byron Young, director of the Kentucky Neuroscience Institute at UK, told a group of neurological surgeons gathered in Orlando, Fla., patients in the UK study moved faster and had improved balance and better control of their movements.

But in late June, Amgen Inc., the developer and patent owner of the drug, announced that an early analysis of a larger, Phase II GDNF study, conducted at several different sites around the country, "showed no clinical improvement compared to a placebo."

Two months later, the drug company announced it was halting the study, and it demanded that all patients immediately stop receiving GDNF because of newly discovered safety issues.

That has led some of the 10 patients in the UK study -- most of whom live in Central and Eastern Kentucky -- the five study participants in Britain and the 34 patients from the Phase II trial to band together in protest.

They've set up a Web site to share testimonials about the positive effects of GDNF and are blanketing Amgen with letters asking that the company restart the study, or at least allow those who were in the study to take the drug.

Hope for 'a normal life'

One of those people is Roger Thacker.

During more than a year on GDNF, Thacker, 65, said he went from constant stiffness and pain to driving tractors on his Versailles farm and planning major trips.

Now that he's off GDNF, "every day seems to get a little tougher," Thacker said.

"Things we forgot we dealt with before are coming back now," said his wife, Linda.

But the couple remains confident.

"I'm anticipating going back on the product, and I'm anticipating a normal life," he said.

Researchers at UK aren't giving up hope for GDNF either.

"We think the drug really has a lot of promise," said Don Gash, chairman of UK's Anatomy and Neurobiology Department.

Safety concerns

Amgen officials have said they're concerned that the drug is unsafe, but they did not return calls for this article.

Some monkeys suffered brain damage after receiving GDNF. And some human subjects developed antibodies to the drug, leading to fear that the antibodies might attack cells in other parts of the patients' bodies that naturally produce GDNF.

However, the UK research-ers think those hurdles might be overcome.

"It's something that should be looked at, but at the present time we have no clinical grounds to say this should stop clinical use of these 10 patients," said Greg Gerhardt, director of UK's Morris K. Udall Parkinson's Disease Research Center of Excellence.

The monkeys that suffered brain damage were given very large doses of the drug, noted Dr. John Slevin, principal investigator on the UK study.

"The toxicity in the monkeys that was seen has not been replicated by any other lab to date," he said.

Gash said it is "very common" for people to develop antibodies to protein drugs, but that those antibodies rarely cause a problem for patients.

"The patients in our study have moderate to late-stage Parkinson's. Their clock is ticking," Slevin said. "Even if they were to develop antibodies, they say 'I'm more worried about dying from Parkinson's than potential effects of that antibody.'"

'The desperate people'

Some patients have speculated -- and Amgen has denied -- that money is at the heart of the company's decision to stop human testing of GDNF.

Amgen is "much more worried about losing money" than about safety, said Long Island resident Elaine Suthers, whose husband was in the study at New York University. Amgen needs a large market to make money on the drug, and the safety concerns would limit the market for an already-specialized drug, Suthers reasons. "This is a very invasive procedure. There aren't too many people who will want this ... It's the desperate people who will want it."

Eddie Abney, 48, of Berea wants it.

He has had Parkinson's for eight years, and was the last of the 10 UK patients to have the pump implanted.

"It's so hard to focus on the holidays, enjoying time with our families, being able to go shopping for our children, grandchildren, because this disease controls every aspect of your life," he wrote in a recent letter to Amgen. "I've spoken with my doctors about alternatives and there aren't any drugs out there that show the promise that the GDNF does."

Researchers are hopeful, but not optimistic, that Amgen will permit those who had been getting GDNF to have it again.

Under U.S. Food and Drug Administration rules, patients in discontinued drug trials can petition to continue receiving the drug, but certain conditions must be met.

In this case, Amgen is reluctant to give the drug to patients because they could sue if they suffered negative side effects, Gerhardt said.

"The reality is that Amgen feels this is a liability issue," he said.

Even if the patients signed a waiver saying they would not sue, the company could still be at risk.

"We've begun talking with Amgen about the possibilities," Slevin said. "When the solution will be arrived at, I have no idea."

'It just gets worse'

In the meantime, the patients' pumps are being injected with saline to keep them from shutting down.

"I've seen a lot of difference," since the GDNF stopped, said Jim Day, a 69-year-old Nich-olasville resident who was diagnosed with Parkinson's 14 years ago. "I'm back where I started from.

"I freeze up, I can't move sometimes. ... With GDNF I was driving out for groceries, now I'm going back the other way. It progresses, it doesn't stop, it just gets worse."

And Webster, who installed water lines to his father-in-law's home last summer, is trying to figure out how he's going to gather the strength to fix the water pipes that burst in his Irvine home this week.

"They're sentencing me to a life of pain and misery," he said.

Reach Karla Ward at (859) 231-3314; 1-800-950-6397, Ext. 3314; or kdooley@herald-leader.com.