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Patients in Test Won't Get Drug, Amgen Decides
By ANDREW POLLACK

A small group of people with Parkinson's disease had been pleading for months with the biotechnology company Amgen: Let them resume taking an experimental drug that the patients said had helped them but which the company said was ineffective and possibly dangerous.

Yesterday Amgen gave its answer: no. The company said it would not make the drug available to the four dozen patients who had participated in its clinical trials, even though the Food and Drug Administration had left the door open for it to do so.

Company executives said that besides exposing the patients to unnecessary risks, to let them continue treatment would only generate false hopes. It might also ultimately hinder development of improved versions of the drug, Amgen said.

"I know this will be received by the patients in a devastating way," Kevin W. Sharer, chief executive of Amgen, said in an interview, describing the verdict as "the hardest decision I've made in my life." But, he added, "we're trying to do the right thing for the most people."

Some patients, along with their family members and doctors, reacted swiftly and angrily, as did some patient advocacy groups.

"They have every reason in the world to give this medication to the patients, and they're not," said Kristen Suthers, whose father had received the drug and who has been one of the main organizers of the patient protest. "To be able to decide whether people are going to suffer - I just wish that I'd never heard of the company."

She said the condition of her father, Robert Suthers of Huntington, N.Y., had improved to the extent that he could walk two miles while on the drug, but now can no longer even bathe himself.

The controversy over the drug raises the question of whether drug companies are obligated to continue providing drugs to participants in clinical trials, even after the trials are ended. In this case, to receive the drug the patients had to undergo surgery to have catheters implanted in their brains and pumps in their abdomens.

"We think there is kind of a moral pact that one makes with a company in these situations that gives the patients a privilege of having continued access to treatment," said Robin Anthony Elliott, executive director of the Parkinson's Disease Foundation.

But Dorothy E. Vawter, associate director of the Minnesota Center for Health Care Ethics, said the question was "not a settled area of research ethics at all and is raising its head more and more all the time." She said an obligation to provide drugs to patients indefinitely after trials end

could discourage drug development.

Amgen's decision reverberated beyond the patients in the trials because the drug, called glial cell line-derived neurotrophic factor, or GDNF, had the potential to stall or even reverse the progression of the disease rather than just reduce the symptoms, as the currently available Parkinson's drugs do.

"As someone with Parkinson's disease who for four years has had GDNF as my big hope, it's absolutely devastating," Tom Isaacs, co-founder of the Cure Parkinson's Trust in England, said of Amgen's decision. Mr. Isaacs walked around the coast of Britain, more than 4,000 miles, to raise money for Parkinson's research, planning, he said, to devote much of that to studies of GDNF.

In initial trials in England and Kentucky involving a total of 15 patients who knew they were getting the drug, virtually all experienced reduction of the tremors and rigidity that characterize the disease, and in some cases the improvements were substantial. But a subsequent trial involving 34 people who did not know whether they were getting the drug or a placebo, indicated that the drug did not prove meaningfully better than the placebo.

Amgen concluded that the positive results in the earlier trials represented a placebo effect, something that is known to occur in Parkinson's trials. Moreover, it said, it found that some monkeys given high doses of the drug had developed potentially serious brain damage. So last summer the company stopped the trials and ordered all patients taken off the drug.

Some doctors involved in the trial, however, have argued that the unsuccessful trial was poorly designed and that the drug worked. They also discounted the findings in monkeys, saying the animals had received a much higher dose than the patients.

Amgen executives and some of the investigators met with the F.D.A. in January. According to the company, the agency said that safety issues would preclude the drug from being given to new patients but that it would consider allowing Amgen to resume treating the existing patients.

Amgen executives said they held many meetings among themselves and talked with outside experts and ethicists. In the end, the executives said, they decided they had to stick with the scientific evidence that the drug might be dangerous and had not been proved effective.

Mr. Sharer said another factor was that if the drug supply were resumed and some patients experienced a placebo effect they attributed to the drug, pressure would only grow on the company to start treating even more patients. "We couldn't find a way to contain this medicine to just these 40 or 50 patents," he said.

He said the company was committed to GDNF and hoped to begin another trial, perhaps delivering the drug by another method, a year or two from now, if the safety issues can be resolved.

"The best thing to do for all patients is to do a proper development of GDNF," Mr. Sharer said. He said that money was not a factor in the

decision and that concerns about the company's legal liability had not been an insurmountable barrier.

Amgen executives also said that there was already an approved therapy, deep brain stimulation, that could help alleviate the symptoms of the patients from the clinical trials.

An ethicist consulted by Amgen, Arthur Caplan of the University of Pennsylvania, said he agreed with the company. Patients "are not in a position, even though they are the recipients, to really understand what is going on in terms of animal signals that may harm them," Mr. Caplan said. "And what they interpret as positive might be colored by hope."

A similar stance was taken by John G. Nutt, a professor of neurology at Oregon Health and Science University who treated four patients in the trial; none of them benefited. He said that four of the patients in the trial who were among those showing the greatest benefits had turned out to be taking the placebo. "Should those patients be offered placebo?"

In contrast, doctors at the University of Kentucky who conducted one of the early trials, criticized Amgen's decision. So did one of the patients treated in that trial.

The patient, Bob Green, 51, of Wilmore, Ky., said GDNF had allowed him to dress himself, get out of bed by himself and even drive on occasion. "So many things that people consider trivial are major to those of us who lack those abilities," he said. Now off the drug, he said his condition was deteriorating.

"I think it's a sad commentary on Amgen's outlook on life, especially as it pertains to us who readily put ourselves on the line to test the medication," he said. "We went through the surgery thinking it might offer hope for us and for others."