# *Panel Says That Innovative Sickle Cell Cure Is Safe Enough for Patients*

The decision by an advisory committee may lead to Food and Drug Administration approval of the first treatment for humans that uses the CRISPR gene-editing system.

**By Gina Kolata**
Gina Kolata has reported on gene therapy for nearly 30 years and on sickle cell disease since 2018.

Oct. 31, 2023, 5:14 p.m. ET

A panel of experts said on Tuesday that a groundbreaking treatment for sickle cell disease was safe enough for clinical use, setting the stage for likely federal approval by Dec. 8 of a powerful potential cure for an illness that afflicts more than 100,000 Americans.

The Food and Drug Administration had previously found that the treatment, known as exa-cel and jointly developed by Vertex Pharmaceuticals of Boston and CRISPR Therapeutics of Switzerland, was effective. The panel's conclusion on Tuesday about exa-cel's safety sends it to the F.D.A. for a decision on greenlighting it for broad patient use.

Exa-cel frees patients from the debilitating and painful effects of this chronic, deadly disease. If approved, the Vertex product would be the first medicine to treat a genetic disease with the CRISPR gene-editing technique.

It could also be the first of a series of new options to cure the excruciating illness. By Dec. 20, the F.D.A. will decide on a second potential cure for sickle cell, a gene therapy devised by the company Bluebird Bio of Somerville, Mass.

Sickle cell disease is caused by a gene mutation that makes blood cells misshapen, so that they resemble sickles or crescents. It affects millions of people worldwide, most of whom have African ancestry. The misshapen cells get stuck in blood vessels, causing strokes, organ damage and episodes of agonizing pain as muscles are starved of oxygen.

Sickle cell's toll starts early in life. Evelyn Islam of Milwaukee, now 8, had 22 blood transfusions and had to have her spleen removed before she was 3. "Gene therapy is our last hope for a cure," said her mother, Melissa Nicole Allen.


Ashley Valentine, a co-founder of the national advocacy group Sick Cells, at her parents' home in Lisle, Ill. Her brother Marqus, pictured on the wall, died in 2020.
Mustafa Hussain for The New York Times

But the new gene therapies will come too late for many.

Ashley Valentine, a co-founder of the national advocacy group Sick Cells, had to take three months off from work in 2016 to help her brother Marqus deal with symptoms of sickle cell. When he had a hip replacement in 2018, her father ended up accepting a layoff from his job to help care for him.

“And that’s just us,” she said.

Marqus died in 2020, at age 36, from a stroke caused by sickle cell.

New treatments like the one that was endorsed on Tuesday are expected to cost millions of dollars per patient, though Vertex has not yet said what it will charge. But lifelong care for patients with the disease is also enormously expensive, costing the health care system an estimated $3 billion a year.

It’s not yet clear how many people will seek the new therapy. The new therapies are also not easy to endure and come with hardships for patients, who will have to undergo chemotherapy and spend more than a month in the hospital. Family members are affected too — they may need to take time off work during the most intensive phase of the treatment.

Additionally, most Americans with sickle cell are Black and may not trust a health care system that has often failed to provide the most basic preventive and therapeutic care for those with the disease. Some with sickle cell are anxious about undergoing a medical treatment that is on the cutting edge of biotechnology.

But for doctors who have spent years watching patients suffer, and many parents who have seen their children endure years of agony, there is elation at what lies ahead.

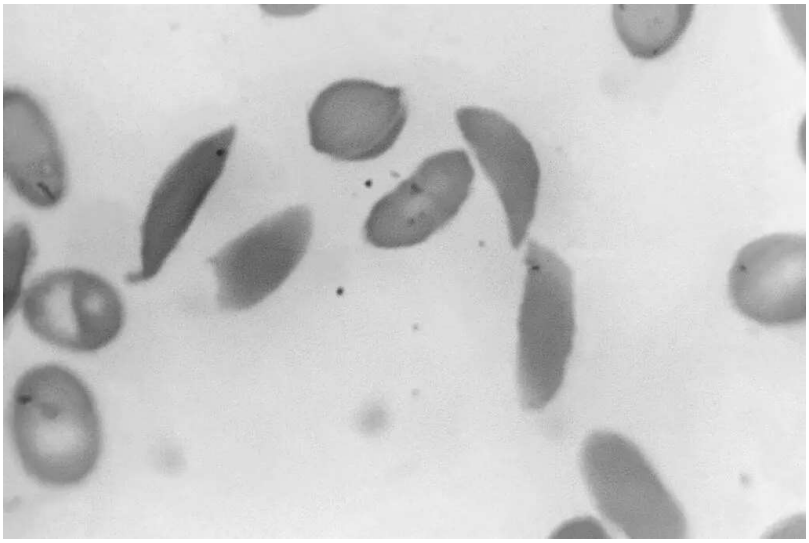
“We are finally at a spot where we can envision broadly available cures for sickle cell disease,” said Dr. John Tisdale, director of the cellular and molecular therapeutics branch at the National Heart, Lung and Blood Institute and a member of the advisory committee.

Dana Jones of San Antonio wants her daughters Kyra, 18, and Kami, 20, to have a chance at one of the new therapies. Both had strokes that left them with learning disabilities — injuries that could probably have been avoided if they had been given a screening test and treatment long known to prevent nine out of 10 strokes in children with the disease. Kyra is now in intensive care as doctors try to control her pain.

Ms. Jones is overwhelmed by the possibility that her daughters could be cured.

“It is my prayer that Kami and Kyra can be cured of this awful disease and finally be able to truly live,” she said.

**A New Treatment and a New Technology**



Sickle cell disease is caused by a gene mutation that makes blood cells misshapen. The misshapen cells can get stuck in blood vessels, causing strokes, organ damage and episodes of agonizing pain. F. Gilbert/CDC, via Associated Press

The cause of sickle cell has been known for nearly 70 years, but research lagged, a situation many say occurred at least in part because so many patients were Black and from poor and working-class families.

There are a number of treatments to reduce sickle cell's impact. Some patients are able to get bone marrow transplants that can cure the condition. But that requires finding a donor and, after the transplant, taking drugs to prevent the body from rejecting the foreign cells.

In recent years, a number of biotechnology companies have tried novel approaches. While Bluebird Bio is advancing its gene therapy technique, Vertex and CRISPR Therapeutics focused on the gene-editing system CRISPR-Cas9, which can home in on specific areas of DNA and turn genes on or off. CRISPR has allowed researchers to disable genes to assess their importance in biomedical research. But until now it has not been used as a treatment for patients with a genetic disease.

To treat sickle cell, CRISPR snips a piece of DNA in bone marrow stem cells. That frees a blocked gene to make a form of hemoglobin that normally is produced only by a fetus. The fetal gene directs the production of hemoglobin that does not form into the sickle shape. In clinical trials, patients no longer had the complications of sickle cell disease and no longer needed blood transfusions.

But there is a concern that CRISPR could inadvertently snip a piece of DNA in the wrong part of a patient's genome. That might disrupt a gene and cause a blood cancer.

No such issues have turned up in the clinical trials, but the Vertex trial involved only 44 patients, and just 30 have been followed for at least 16 months. The company did extensive comparisons of patients' DNA with that of people in large databases asking how likely such CRISPR misfires could be.

Vertex said it plans to follow clinical trial patients for 15 years. The company's data were sufficiently reassuring that the expert committee said on Tuesday they saw no reason to hold the treatment back.

There can always be additional studies, noted committee member Alexis Komor, a professor of chemistry and biochemistry at the University of California, San Diego. But, she said, that would be "expecting perfection at the expense of progress."

Dr. Joseph Wu of Stanford added, "We all agree that the benefits outweigh the risks. These patients are quite sick and this is a good therapy."

Scot Wolfe of the University of Massachusetts Chan Medical School said, "We want to be careful not to let the perfect be the enemy of the good."

"There is a huge unmet need," he added.

**If It's Safe, Who Gets It?**

Vertex Pharmaceuticals' headquarters in Boston. Bill Sikes/Associated Press

Vertex estimates that 20,000 people could be eligible for its treatment, and says Medicaid and private insurers have suggested a willingness to pay for it.

"There is almost no way they could *not* pay," said Dr. David Williams, chief of the division of hematology and oncology at Boston Children's Hospital.

Dr. Williams, who has consulted for Vertex and Bluebird Bio, added that insurers pay "$3 million a pop" for other gene therapies produced by Bluebird Bio for the diseases thalassemia and adrenoleukodystrophy. With sickle cell, and its large number of Black patients, he said, there is an issue of "equity in access and the tremendous medical need."

Some people with the disease may not be eligible, depending on the F.D.A.'s decisions. They could include young children with sickle cell and older patients whose bodies have been so damaged that the treatment could pose heightened risks.

Kevin Wake of Kansas City, Mo., hopes he is not too old, at 55, or too damaged. He has had three strokes caused by the disease.

The treatments, though curative, are difficult.

Patients first have eight weeks of blood transfusions followed by a treatment to release bone marrow stem cells into their bloodstream. The stem cells are then removed and sent to the companies to be treated. Next, patients receive intense chemotherapy to clear their marrows for the treated cells. The treated cells are infused back into the patients, but they have to remain in the hospital for at least a month while the new cells grow and repopulate their marrows.

That treatment "cannot be delivered at most hospitals," said Dr. Alexis Thompson, chief of the division of hematology at Children's Hospital of Philadelphia, who consults for Vertex.

Another issue is how quickly Vertex can ramp up production. Each patient's cells must be treated individually in a sterile environment, an arduous prospect.

Stuart Arbuckle, executive vice president and chief operating officer at Vertex, is confident. "We are launch ready," he said. But he added that he did not expect a huge wave of patients immediately.

"This is a pretty big decision for a patient to go through," Mr. Arbuckle said.


Dana Jones with her daughter Kyra, now 18, in 2020. Kyra and her sister Kami have had strokes that caused them to have learning disabilities, and Kyra is currently in intensive care as doctors try to control her pain. Ilana Panich-Linsman for The New York Times

One of the Vertex clinical trial patients, Marie-Chantal Tornyenu, 22, who is a senior at Cornell University, said patients also had to be prepared for “mental adjustment” after treatment.

Ms. Tornyenu said she no longer had the pain crises that plagued her, especially in high school when she was hospitalized nearly every month.

But she has spent much of her life taking precautions and worrying about pain and complications from sickle cell. Those habits are hard to break.

“It’s a major learning curve from having sickle cell my whole life,” she said. “I’m still struggling with that mind-set — ‘sickle cell is you.’”

**Gina Kolata** writes about science and medicine. She has twice been a Pulitzer Prize finalist and is the author of six books, including “Mercies in Disguise: A Story of Hope, a Family's Genetic Destiny, and The Science That Saved Them.” More about Gina Kolata