# Researchers publish final results of key clinical trial for gene therapy for sickle cell disease

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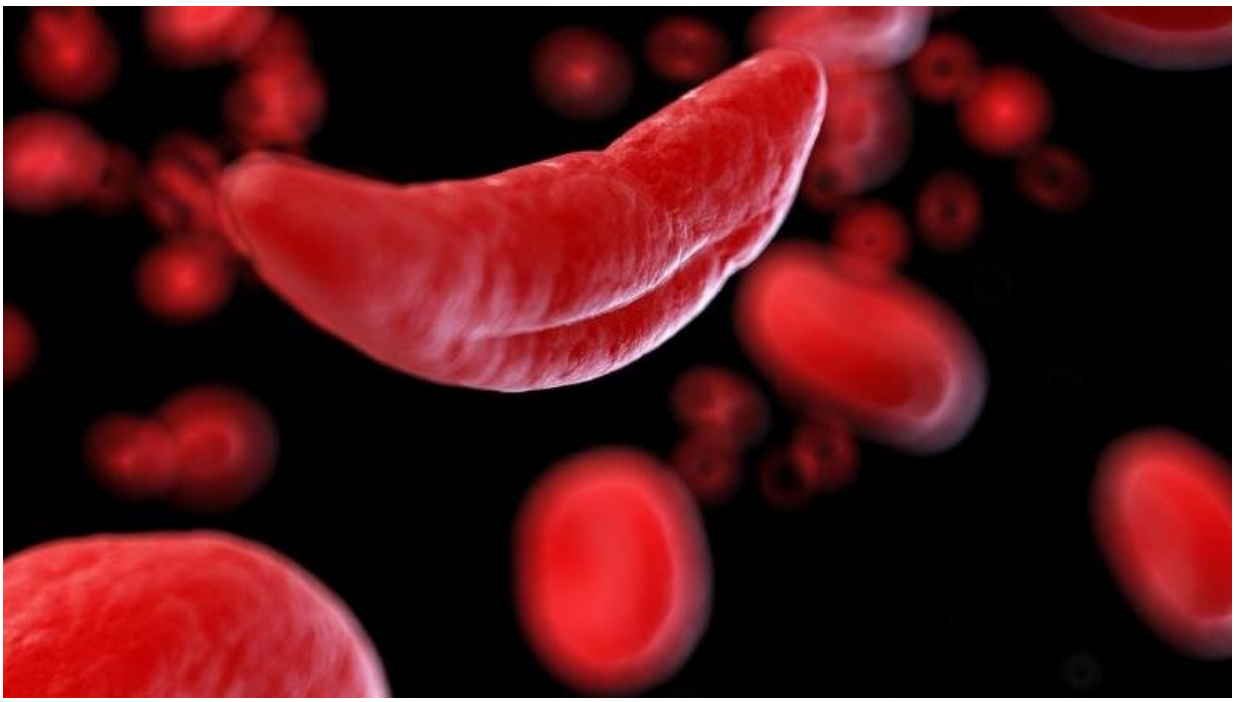

Credit: National Institutes of Health

In a landmark study, an international consortium led by researchers at Children's Hospital of Philadelphia (CHOP) published the final results of a key clinical trial of the gene therapy CASGEVY (exagamglogene autotemcel) for the treatment of sickle cell disease in patients 12 years

and older with recurrent vaso-occlusive crises (VOCs).

The study found that 96.7% of patients in the study did not have any vaso-occlusive crises (VOCs)—a blockage that results in lack of oxygen and painful episodes—for at least one year, and 100% were able to remain hospitalization-free for the same length of time.

The findings, published in the *New England Journal of Medicine*, provide the complete details of the critical clinical trial that led to the FDA approval of CASGEVY for the treatment of sickle cell disease in December 2023.

Sickle cell disease is a lifelong condition that causes intense pain due to deformed blood cells that can cause blockages in blood vessels. This can also lead to strokes, organ damage, and shortened lives.

Researchers have been studying the use of gene therapy and CRISPR technology to edit portions of DNA in people with inherited or genetic disorders, like sickle cell disease. In the case of sickle cell disease, the CASGEVY process edits DNA within the patient's own cells and enables the patient to produce a different form of hemoglobin in their red blood cells.

Clinical trials at CHOP and other sites have shown that successful gene editing can prevent cells from developing the distinctive crescent shape apparent in sickle cell disease and have eliminated pain episodes in almost all patients. CASGEVY was the first FDA-approved therapy developed with CRISPR technology.

"In this clinical trial, sickle cell patients who were having significant issues with their disease began to see their problems resolve within months and improve their quality of life significantly," said senior study author Stephan A. Grupp, MD, Ph.D., Section Chief of the Cellular

Therapy and Transplant Section, Inaugural Director of the Susan S. and Stephen P. Kelly Center for Cancer Immunotherapy, and Medical Director of the Cell and Gene Therapy Laboratory at CHOP.

Grupp was also one of the principal investigators in the clinical trials that led to the approval of CASGEVY and the leader of the study's steering committee.

The researchers conducted the CLIMB SCD-121 trial, a Phase III, single-arm, open-label study of exa-cel in patients between 12 and 35 years old with sickle cell disease and at least two severe VOCs in each of the two years before screening. The key primary endpoint of the study was a proportion of patients without severe VOCs for at least 12 consecutive months, with a secondary endpoint of patients who were free from inpatient hospitalization for severe VOCs for at least 12 consecutive months.

A total of 44 patients received exa-cel with a median follow up of 19.3 months. In a total of 30 patients with sufficient follow-up data to be evaluated, 29 (96.7%) were free of VOCs for at least 12 consecutive months.

This information is an update for the US Prescribing Information for CASGEVY, which includes an evaluation of 31 patients resulting in a response rate of 93.5%. The safety of treatment was comparable to treatment with hematopoietic and progenitor stem cells, and no malignancies were reported as a result of treatment.

Additionally, the results of a clinical trial on the efficacy of exa-cel for the treatment of β-thalassemia were also published in the *New England Journal of Medicine*. The preliminary results of the trial led to the FDA approval of CASGEVY for transfusion-dependent β-thalassemia in January 2024. Grupp was also one of the principal investigators for this

clinical trial.

**More information:** Haydar Frangoul et al, Exagamglogene Autotemcel for Severe Sickle Cell Disease, *New England Journal of Medicine* (2024). DOI: 10.1056/NEJMoa2309676

Locatelli et al, Exagamglogene Autotemcel for Transfusion-Dependent β-Thalassemia, *New England Journal of Medicine* (2024). DOI: 10.1056/NEJMoa2309673.

Provided by Children's Hospital of Philadelphia