Researchers identify safety of a potential new treatment to manage complications from sickle cell disease

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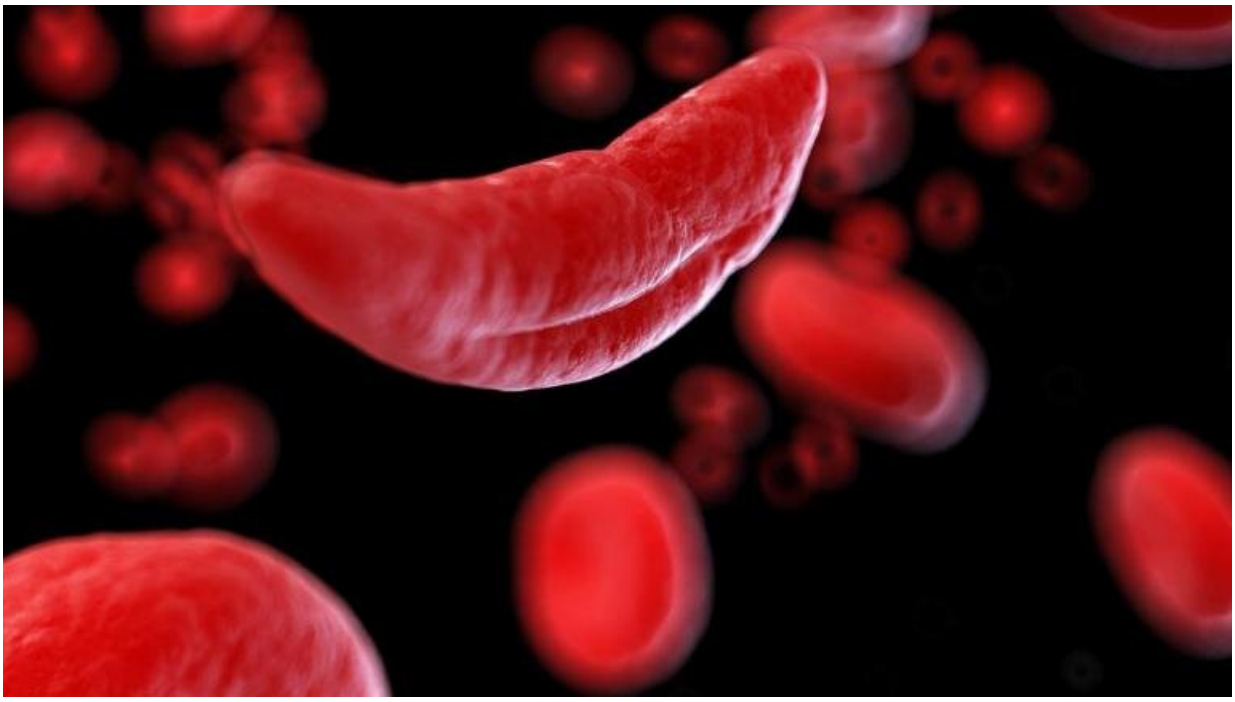

Credit: National Institutes of Health

A drug approved to treat pulmonary arterial hypertension may be

effective at managing hypertension and end-organ damage in patients with sickle cell disease, according to a new study published in *Lancet Haematology*.

An early-phase randomized clinical trial involving 130 patients with sickle cell disease found that the drug, called riociguat, was found to be safe to use and well tolerated in these patients and significantly improved their blood pressure. Preliminary efficacy data suggested the medication might improve heart function.

An estimated 100,000 Americans have sickle cell disease, and the disease occurs in about 1 out of every 365 Black or African-American births, according to the Centers for Disease Control and Prevention.

People with sickle cell disease are at high risk for vascular complications that can lead to pulmonary hypertension, stroke, and kidney failure, as well as severe pain when red blood cells block blood flow through tiny blood vessels in the chest, abdomen, and joints. These complications can be worsened by hypertension.

Unfortunately, previous research found that sildenafil, an effective treatment for pulmonary hypertension, caused unacceptable side effects in patients with sickle cell disease. It found that those who took this drug experienced high levels of pain that caused increased admissions to the hospital compared to those who took a placebo treatment.

This new study was designed to test the safety of riociguat and how well it works in preventing or reducing clinical complications for patients with sickle cell disease.

In the study, patients with sickle cell disease and mild hypertension or

protein in their urine (an early sign of kidney disease) were randomly assigned to receive either riociguat or a placebo in a double-blind clinical trial.

Both groups received the study drug at a starting dose of 1 milligram, which was gradually increased up to 2.5 milligrams and taken three times a day for 12 weeks. The researchers found that among the participants who took riociguat, 22.7 percent experienced at least one serious adverse event related to the treatment. In comparison, in the group that received the placebo, 31.3 percent of participants had at least one serious adverse event during the study.

The differences were not statistically significant. There were no differences between the two groups in the rates of pain severity, pain interference in their daily lives, and vascular events related to their sickle cell disease. When it comes to the effectiveness of the drug treatment, participants who took riociguat had their blood pressure drop by 8.20 mmHg, while those who took a placebo only saw a decrease of about 1.24 mmHg.

The result was highly statistically significant, meaning riociguat was much more effective at lowering blood pressure compared to the placebo, with a difference of approximately 6.96 mmHg. In summary, riociguat was found to be safe and led to a significant improvement in blood pressure over the duration of the study.

"Our results are encouraging and open the door to larger clinical trials involving this class of drugs in patients with sickle cell disease who have pulmonary hypertension or kidney disease."

"Having a drug that's easy to tolerate can help them better manage their blood pressure and help prevent serious complications down the road," said study leader Mark T. Gladwin, MD, who is the John Z. and Akiko

K. Bowers Distinguished Professor and Dean of UMSOM, and Vice President for Medical Affairs at University of Maryland, Baltimore.

More information: Mark T Gladwin et al, Riociguat in patients with sickle cell disease and hypertension or proteinuria (STERIO-SCD): a randomised, double-blind, placebo controlled, phase 1–2 trial, *The Lancet Haematology* (2024). DOI: 10.1016/S2352-3026(24)00045-0

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