Protocol Plain Language Summary

A study of the effects and safety of vericiguat in children with heart failure

Protocol Title: A Phase 2/3 Randomized, Placebo-Controlled, Double-blind, Clinical Study to Evaluate the Efficacy, Safety, and Pharmacokinetics of Vericiguat in Pediatric Participants with Heart Failure due to Left Ventricular Systolic Dysfunction (VALOR)

Why is this study needed?

Heart failure (HF) is a serious disease that not only affects the quality of life of a person but also raises the chance of hospitalization and death. In HF, the heart does not pump enough blood to the body. Most of the current treatments used for HF in children are approved for HF in adults. Doctors use these treatments in children because HF in children is likely to be similar to HF in adults. Past studies in adults found that vericiguat lowered the chance of hospitalization and death from HF. Vericiguat is approved for adults with HF.

In this study, researchers want to learn if **vericiguat** lowers the severity of HF in children based on a blood test called **NT-proBNP**. NT-proBNP measures the blood level of a protein that the heart makes during HF. Blood levels of NT-proBNP go up when HF gets worse and go down when HF is controlled.

Who will take part in this study?

About 342 children with chronic (long-lasting) HF will be in this study. Children in the study will:

- Be more than 28 days to less than 18 years of age
- Have HF symptoms caused by left ventricular systolic dysfunction, a condition when the left ventricle of the heart cannot pump out enough blood
- Be on stable treatment for HF

How is this study designed?

Children will be in the study for up to 58 weeks. Children will be assigned by chance to take vericiguat or a placebo. Using a placebo helps researchers better understand the effects of a study medicine. Neither the children nor the researchers will know which treatment will be given (double-blinded study).

Children will give blood samples, an electrocardiogram (ECG) and bone x-rays will be taken, and children or their parents will answer a set of questions before, during, and after the treatment. Children older than 6 years will also have hearing tests.

What treatments are being studied?

Children will be assigned to take one of the following once a day for 52 weeks:

- Vericiguat, taken by mouth as a tablet or liquid
- Placebo, taken by mouth as a tablet or liquid (a placebo looks like a study medicine but has no actual study medicine in it)

The starting dose (amount) and formulation (tablet or liquid) of vericiguat depend on the child's weight. The dose will go up 1 or 2 times during the study depending on the child's blood pressure. Researchers will stop or lower a child's dose of vericiguat if they have low blood pressure.

What are the goals of this study and how will they be measured?

Main goal	How it will be measured
Learn if vericiguat lowers the level of NT-proBNP in the blood compared to placebo to 16 weeks of treatment	Change in the blood level of NT-proBNP from before treatment to week 16

Other goals	How they will be measured
Learn if vericiguat lowers the level of NT-proBNP in the blood compared to placebo to 52 weeks of treatment	Change in the blood level of NT-proBNP from before treatment to week 52
Learn how well vericiguat lowers the chance of serious heart problems compared to placebo	The average length of time from the start of treatment until any of these happen to children in the study: • Death due to heart problems • Hospitalization due to HF • HF gets worse
Learn about the safety of vericiguat and how well children managed (tolerate) the treatment compared to placebo	• Number of children who have at least 1 adverse event during the study. An adverse event is a medical problem that happens or worsens during a study and may or may not be caused by the treatment • Number of children who stop taking the study treatment due to an adverse event
Learn how the body processes and removes vericiguat	Blood tests to measure: • the level of vericiguat in the body over time (AUC) • the time it takes to decrease the level of vericiguat in the blood by half (t ½) • the time it takes for vericiguat to be removed from the body (F/CL).

What are the possible benefits and risks?

Children in this study may or may not have improvement in their HF. This study has a Data Monitoring Committee that oversees the study's overall risk and benefit. If the committee decides that the study treatment is not safe, the study can be stopped.

More details about benefits and risks for children in this study may be found in the protocol, Investigator Brochure, and Informed Consent Form.