Successful outcome prompts early end to sickle cell anemia clinical trial

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Conclusive data show that hydroxyurea therapy offers safe and effective disease management of sickle cell anemia (SCA) and reduces the risk of stroke, prompting early termination by the National Heart Lung and Blood Institute (NHLBI) of a key clinical trial studying the drug's efficacy.

NHLBI officials issued the announcement today, about one year before the study was originally scheduled to end. Going by the title TWiTCH (TCD With Transfusions Changing to Hydroxyurea), the Phase III randomized clinical trial at 25 medical centers in the U.S. and Canada compared standard therapy (monthly erythrocyte transfusions) with the alternative (daily hydroxyurea) for children with elevated transcranial Doppler (TCD) velocities and high risk of stroke.

"Early results indicate that TWiTCH is a success. Hydroxyurea works as well as blood transfusions to lower TCD velocities, which lowers the risk of the child having a stroke," said Russell E. Ware, MD, PhD, principal investigator of the study and director of Hematology at Cincinnati Children's Hospital Medical Center, which served as the study's Medical Coordinating Center.

"A group of outside experts has been reviewing the TWiTCH data every few months to ensure the safety of children in the clinical trial and to monitor the data," Ware explained. "This group met recently and after careful consideration of the interim data results, recommended that the study be stopped since hydroxyurea worked as well as transfusions to

lower TCD velocities." The NHLBI and National Institutes of Health (NIH) agreed with the recommendation.

"No child should ever suffer a stroke, which is why it was so important for the NHLBI to support the TWiTCH trial," said Gary Gibbons, MD, director of the NHLBI. "This critical research finding opens the door to more treatment options for clinicians trying to prevent strokes in children living with the sickle cell disease."

The study enrolled its first patient in September 2011 and included children between ages 4 and 16 years with sickle cell anemia and abnormally elevated TCD velocities, which increases their risk of developing a stroke. The current standard therapy for children with elevated TCD velocities is monthly blood transfusions. A total of 121 children were randomized: half received the standard therapy of transfusions while the other half received the alternate treatment with daily hydroxyurea, which has not yet been approved for children with sickle cell anemia.

The clinical data-collection portion of the study was originally scheduled for 24 months, but collection is now being stopped early, after only half of the children have completed the treatment phase.

"We did not know if hydroxyurea would reduce the risk of stroke as well as transfusions, so TWiTCH was an important research study," said Barry R. Davis, MD, PhD, principal investigator for the Data Coordinating Center at the University of Texas Health Science Center at Houston (UTHealth) School of Public Health. "The study has now shown that hydroxyurea has a similar benefit as transfusions, so the study is closing early since the main research question has been answered."

An important reason for testing hydroxyurea is that the current standard therapy of monthly blood transfusions to reduce stroke risk can lead to

problems such as antibody formation and iron overload, which are increasingly recognized as a source of morbidity in young patients with SCA.

Over the past decade, the laboratory and clinical efficacy of hydroxyurea has been demonstrated in children and adults with SCA. Originally developed as a drug to treat cancer and infections, hydroxyurea boosts fetal hemoglobin production in SCA, which prevents the red blood cells from acquiring the sickled shape that fuels the many complications. Hydroxyurea has been previously shown to have clinical efficacy for a variety of sickle-related complications, but TWiTCH is the first Phase III trial that demonstrates its benefits for children with cerebrovascular disease and increased stroke risk.

Provided by Cincinnati Children's Hospital Medical Center