UT SOUTHWESTERN MEDICAL CENTER NEWS

Media Contact: Aline McKenzie
214-648-3404
aline.mckenzie@utsouthwestern.edu

Poor response to anti-anemia drug predicts higher risk of heart disease or death, UT Southwestern researchers find

DALLAS – Dec. 29, 2010 – Patients with diabetes, kidney disease and anemia who don't respond to treatment with an anti-anemia drug have a higher risk of cardiovascular disease or death, researchers at UT Southwestern Medical Center have found.

The results suggest that testing such patients' responsiveness to the drug and keeping blood iron levels a little low might reduce their risk, said Dr. Robert Toto, professor of internal medicine and clinical sciences and a senior author of the study, which appeared in the *New England Journal of Medicine.*

"These patients required higher doses and ended up having lower hemoglobin anyway," Dr. Toto said. "The results of this study might lead us in directions that can help."

The results were an unexpected finding of a study on darbepoetin alpha, which stimulates the production of red blood cells to counteract anemia. The drug, manufactured by Amgen, is sold under the name Aranesp.

The study, called the Trial to Reduce Cardiovascular Events with Aranesp Therapy (TREAT) showed that darbepoetin alpha works no better than a placebo for improving cardiovascular and kidney outcomes, but it did lower the risk for blood transfusion and resulted in modest improvement in patient-reported outcomes among people with diabetes, kidney disease and anemia. However, people receiving darbepoetin alpha had nearly a twofold higher risk for stroke. Cancer deaths were also higher among people receiving the drug.

Darbepoetin alpha is one of a class of anti-anemia drugs that mimics erythropoietin, the body's natural hormone that stimulates production of red blood cells.

The combination of type 2 diabetes, chronic kidney disease and anemia affect about 1 million people in the U.S.

TREAT was a double-blinded experiment with a control group that received a placebo. It included 4,038 participants, all of whom had type 2 diabetes, anemia and kidney damage, although not enough to require dialysis. Of these, 1,872 received injections of the drug, and 1,889 received placebo injections.

Participants receiving darbepoetin alpha also received periodic subcutaneous injections of the

(MORE)

drug with the aim of increasing their levels of hemoglobin – a protein in red blood cells that carries oxygen – to a level of 13 grams per deciliter. If someone in the control group dropped to a dangerous hemoglobin level below 9 g/dl, he or she received "rescue therapy" with darbepoetin until the hemoglobin level returned to a level above 9 g/dl.

In analyzing the results, the researchers divided the participants into two groups: those whose hemoglobin levels promptly increased in response to early doses of darbepoetin alpha, and those whose bodies responded less strongly, with hemoglobin level staying low.

The participants who had poor initial responses to the drug had a higher rate of death, heart attack, stroke or heart failure, the researchers found.

The study cannot show whether those people had higher risk for those outcomes because they were in poorer health to begin with, or because of some action of the drug, the researchers stated.

However, it does raise the question of whether treatment for anemia should be customized according to a patient's response to the drug, Dr. Toto said. "Our studies suggest that we might be able to use the initial dose response to identify high-risk groups in future studies," he said.

For instance, if a person's hemoglobin level doesn't improve within one or two months of anti-anemia treatment, it may be better to stop the drug and seek alternative treatment. A state of mild anemia might pose less cardiovascular risk in such a case than continuing or escalating the dose in an attempt to reach a normal hemoglobin level, Dr. Toto said. Conversely, for patients who respond quickly to the drug, treating them until they reach the normal goal range recommended by the Food and Drug Administration appears safer, he said.

Researchers from Brigham and Women's Hospital and Harvard Medical School; Tufts Medical Center; the University of Erlangen-Nuremburg, Germany; the Faculdade de Medicina de São José do Rio Prieto, Brazil; University Medical Center, Groningen, the Netherlands; Northwestern University Feinberg School of Medicine; Health Sciences Centre, St. John's, Canada; Mario Negri Institute for Pharmacologic Research, Italy; Amgen; and the University of Glasgow also participated in the study.

The study was funded by Amgen.

Visit http://www.utsouthwestern.org/heartlungvascular to learn more about UT Southwestern's heart, lung and vascular clinical services, including for cardiovascular illnesses and conditions.

###