MedicalXpress

Engineered clotting protein stops bleeding in most common inherited bleeding disorder

August 3 2015

The first protein engineered to help control bleeding episodes in patients with severe von Willebrand disease (vW disease) has been shown to be safe and effective, according to results of a Phase III trial. Study data were published online today in *Blood*, the Journal of the American Society of Hematology

When a blood vessel becomes damaged, a protein called von Willebrand factor (vWF) helps stop bleeding by guiding clot-forming platelets to the injury. vWF serves as the "glue" that helps platelets stick to a wound. Approximately 1 percent of the general population lacks a sufficient quantity of fully functioning vWF. This results in vW disease, which is characterized by excessive and often hard-to-treat bleeding.

While some patients with vW disease have mild or no symptoms, others have a more severe form of the disease that can be difficult to treat. Until recently, bleeding episodes in individuals with severe vW disease were treated with an infusion of purified vWF, which circulates in combination with factor VIII (FVIII), another clotting protein. While this treatment approach is often effective, the major disadvantage is that vWF is purified from plasma, which has the potential to introduce patients to blood-borne contaminants.

Seeking a more targeted vW disease treatment without the disadvantages associated with blood-derived products, investigators engineered a cell line that expresses the vWF gene to create a consistent, highly active recombinant vWF (rvWF). After preliminary studies, investigators

enrolled 49 patients who had received vWF concentrate treatment for at least one severe vW disease-related bleed within the last 12 months in a Phase III trial to evaluate the efficacy and safety of rVWF. Patients were randomly assigned to one of four treatment arms. In order to observe rvWF's activity at varying doses and in different treatment scenarios, investigators gave patients 50 IU/kg or 80 IU/kg body weight either alone or with engineered FVIII (rFVIII). The majority of patients in the study received as-needed treatment of 40-60 IU rvWF/kg for regular bleeding episodes and up to 80 IU/kg for major bleeds.

Confirming the results of past studies, the activity of rvWF remained the same with and without rFVIII. Investigators observed that patients who received rvWF alone experienced a rapid increase in their naturally produced FVIII. In fact, within six hours after an infusion, patients had produced enough of the protein for proper clotting. This response was sustained through 72 hours post infusion, suggesting that patients who receive rvWF are not likely to require additional rFVIII infusions.

vW disease specialists also rated the recombinant product's ability to control bleeds on a scale of "excellent" to "no response." After 12 months, the specialists had treated 192 bleeding episodes in 22 patients with severe vW disease and rated rvWF as "excellent" (96.9%) or "good" (3.1%) in controlling bleeding. In addition, more than 80 percent of bleeds were resolved with a single rvWF infusion.

"These efficacy and safety data of recombinant vWF represent a major advance in our quest to develop an optimal treatment for people living with vW disease," said lead investigator Bruce Ewenstein, MD, PhD, of Baxalta, Inc. "As this product is specifically designed to be administered without factor VIII, it will allow physicians to dose vWF and FVIII separately and precisely for each individual patient. This treatment strategy has the potential to become the standard of care for patients with severe von Willebrand disease."

Provided by American Society of Hematology