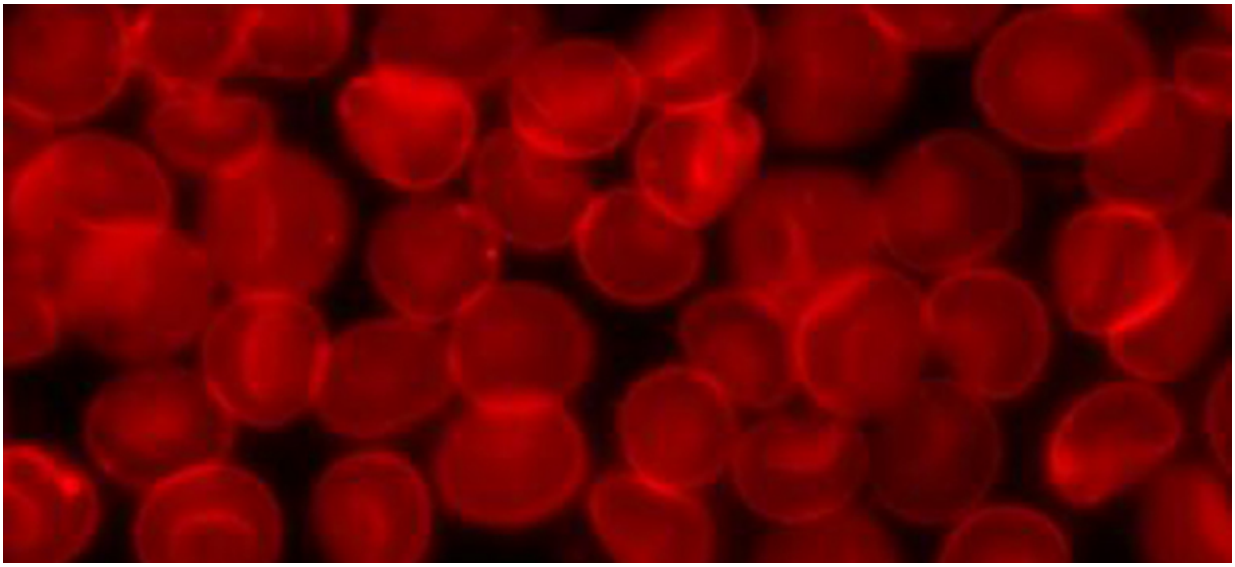
MedicalXpress

Engineered therapy for blood clotting disorder shows early promise

September 14 2017



Credit: Wikimedia Commons

An investigational treatment that mimics a key clotting enzyme is effective, safe, and may one day eliminate the need for blood products for people with the rare, life-threatening blood disease hereditary thrombotic thrombocytopenic purpura (TTP), according to a study published online today in *Blood*, the Journal of the American Society of Hematology (ASH).

Congenital TTP is characterized by blood clots in small blood vessels

throughout the body. If untreated, people with TTP can develop strokes, heart attacks, or kidney damage. Today, the most common therapy for TTP consists of plasma infusions, in which individuals with severe cases of the disease must go to a hospital to receive the blood product from a donor to replenish the missing enzyme in the blood. However, many patients become intolerant to plasma. They develop severe allergic reactions, which make it nearly impossible to treat them. If they can receive treatment, it's under very close supervision and with precautions.

"Today, TTP patients are under-treated because of the complications associated with blood plasma infusions, which has remained the standard treatment for at least half a century," said senior study author Bruce Ewenstein, MD, PhD, of Shire in Cambridge, MA. "Plasma as a source of enzyme replacement is a sledgehammer approach to treatment, but it's the best we have right now."

"Our novel therapy has the potential to be safer, more convenient, and achieve better outcomes," he said.

In people with TTP, the plasma levels of an enzyme known as ADAMTS-13 are very low or missing. This important enzyme helps prevent excessive blood clotting in small blood vessels throughout the body. When ADAMTS-13 is absent or deficient, platelet clumping can occur when it shouldn't and cause organ damage. Researchers have created an engineered form of ADAMTS-13 (BAX 930) to restore the missing enzyme in the blood without the potential complications that can result from human-donor plasma or the inconvenience of a hospital visit. Patients could eventually be able to administer their own infusions at home about every two weeks.

In this Phase I, multi-center clinical trial, researchers investigated the safety, tolerability and pharmacokinetics of BAX 930 in 15 patients diagnosed with severe congenital ADAMTS-13 deficiency. Each patient

received a single dose of BAX 930. The aim was to determine whether this engineered product increased the missing enzyme, ADAMTS 13, in the body and to determine a safe, effective dose for future studies.

In blood samples from these patients, the researchers found that BAX 930 behaved similarly to the endogenous enzyme and restores ADAMTS-13 activity. Specifically, they observed the normalization of the structure of von Willebrand factor, a blood protein that works closely with ADAMTS-13 to help regulate platelet function and clotting. They also observed an improvement in platelet counts, which is a marker of TTP disease activity.

Importantly, BAX 930 was well tolerated in all 15 patients, with no allergic reactions or serious adverse events, and no signs of an immune response to the single infusion.

"What the study shows is that this recombinant protein mimics what we would expect the normal protein to do in patients who do not have congenital TTP," said lead study author Marie Scully, MD, of University College London Hospitals NHS Trust, who is supported by the National Institute for Health Research University College London Hospitals Biomedical Research Centre.

A Phase III trial is set to begin later this year. The study will look at the long-term safety and efficacy at both preventing and treating acute attacks. Study participants will be repeatedly exposed to BAX 930 for 12 months.

"This treatment is a complete game-changer for people with TTP, not only for the patients, but also for clinicians to be able to give the right treatment so that patients have reduced episodes," Dr. Scully said.

Provided by American Society of Hematology