Drug for rare paroxysmal nocturnal hemoglobinuria receives FDA orphan status

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A Penn Medicine-developed drug has received orphan status from the Food and Drug Administration (FDA) this month for the treatment of paroxysmal nocturnal hemoglobinuria (PNH), a rare, life-threatening disease that causes anemia due to destruction of red blood cells and thrombosis. This designation comes less than two months after the European Medicines Agency (EMA) approved the drug for the same status.

Orphan designation for the drug, called AMY-101, will allow Amyndas, the company currently developing the compound, to proceed with expedited clinical development. Amyndas is planning to move AMY-101 into the clinic for first-in-human trials in 2015. AMY-101 is a new way to fight PNH, which is currently only treatable with the most expensive drug available for sale in the United States. The new strategy is based on inhibiting C3, a central component of the oldest part of the human immune system – called "complement"—and could turn out to be less costly and more effective for the majority of patients with this rare blood disorder.

If a drug is approved by the FDA, this special orphan status allows for a seven-year period of market exclusivity from product launch in the United States, and enables an orphan drug's maker to apply for research funding, tax credits for certain research expenses, and assistance for clinical research study design. This status also provides a waiver from the FDA's Prescription Drug User Fee, which authorizes the FDA to collect fees from drug sponsors to expand their staff so that new drugs can be reviewed more quickly.

John Lambris, PhD, the Dr. Ralph and Sallie Weaver Professor of Research Medicine in the Department of Pathology and Laboratory Medicine in the Perelman School of Medicine, developed AMY-101 at Penn, and in 2013 the university licensed it to Amyndas, which is now further developing the compound for application in the clinic.

"Receiving the orphan drug designation from both the FDA and the EMA is an important achievement and a key milestone in the development pathway of AMY-101 and we are optimistic regarding the long-term potential of this potent complement inhibitor," said Lambris. "AMY-101 could represent a significant therapeutic advantage over treatments currently available for PNH."

PNH affects between 1 and 5 per million people and is caused by a defective expression of regulatory proteins on the surface of blood cells, leaving them vulnerable to complement attack. This can lead to premature death of the red blood cells, a process called hemolysis, which results in severe anemia and contributes to a high risk of clotting. AMY-101 tames this inappropriate complement activation and protects cell surfaces from attack.

Although one treatment exists for PNH, one third of patients continue to require blood transfusions to manage their anemia. This non-response is due the accumulation of fragments of complement C3 proteins on the surface of their red blood cells, which are eventually attacked by immune cells. The team investigated the effect of AMY-101 on self-attack and resulting hemolysis using human PNH cells and found it be active.

Provided by University of Pennsylvania School of Medicine