Emicizumab Reduces Bleeding Rates in Hemophilia A with Inhibitors

New study demonstrates efficacy of emicizumab in difficult-to-treat subpopulation of hemophilia A patients

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July 11, 2017 – Patients with hemophilia A with factor VIII inhibitors were less likely to develop bleeding events when treated with prophylactic emicizumab versus placebo, according to the results of a new phase III trial.

Johannes Oldenburg, MD, and colleagues published their findings in a July 10 advance online publication of the *New England Journal of Medicine*.

Hemophilia A affects approximately 320,000 people worldwide. Current treatment for hemophilia A in patients with a high titer of inhibitors includes eradication by inducing immune tolerance or treatment with bypassing agents (recombinant factor VII or activated prothrombin complex).

"The efficacy of bypassing agents remains suboptimal, and both options involve frequent intravenous infusions that depend on adequate venous access; thus, more effective and less burdensome treatments are needed," noted the study authors.

Emicizumab is a recombinant monoclonal antibody that bridges activated factor IX and factor X to restore deficient factor VIII function in patients with hemophilia A. Clinical studies to date have not demonstrated that emicizumab induces the development of inhibitors or that it is affected by the presence of existing inhibitors.

The HAVEN 1 study was an open-label, randomized trial that included 109 males with hemophilia A with inhibitors who had previously received episodic or prophylactic treatment with bypassing agents.

Patients who had previously received episodic treatment were randomized to either emicizumab subcutaneous once-weekly prophylaxis (group A) or placebo (group B). Patients who had previously received prophylactic treatment with bypassing agents were given emicizumab prophylaxis (group C). The primary endpoint was defined as the difference in treated bleeding rates between group A and group B over at least 24 weeks.

Overall, the annualized bleeding rate decreased by 87% with emicizumab therapy (2.9 events in group A versus 23.3 events in group B; $P < 0.001$). Among the 24 patients in group C who had previously received prophylactic bypassing agents, emicizumab prophylaxis demonstrated a 79% lower bleeding rate than the rate with the previous prophylactic bypass agent ($P < 0.001$).

A total of 198 adverse events were reported in the study, with the most common events in treated patients being injection site reactions (15% of patients). Thrombotic

microangiopathy and thrombosis were each reported in 2 patients receiving emicizumab. These patients had also received multiple prothrombin infusions for breakthrough bleeding. No antidrug antibodies were identified.

The authors concluded, “emicizumab may provide a weekly, subcutaneous, prophylactic therapeutic option for patients with hemophilia A with inhibitors.”

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Oldenburg J, Mahlangu JN, Kim B, et al. Emicizumab Prophylaxis in Hemophilia A with Inhibitors [published online July 10 2017]. *N Engl J Med*. 2017. doi: 10.1056/NEJMoa1703068.