

**STATEMENT ON PROPHYLAXIS WITH FEIBA - STUDY RESULTS PUBLISHED IN
*THE NEW ENGLAND JOURNAL OF MEDICINE***

DEERFIELD, ILL., November 2, 2011 – Results from an investigator-initiated study, which evaluated whether prophylactic use of FEIBA [Anti-inhibitor Coagulant Complex] can achieve a decrease in the frequency of joint and other bleeding events in patients with severe haemophilia A and inhibitors compared to on-demand therapy, were published today in *The New England Journal of Medicine*. Patients with severe haemophilia A and inhibitors are at increased risk for serious bleeding complications. Effective strategies to prevent bleeding in inhibitor patients have not yet been established. Prophylaxis, where approved, is used to prevent a bleed and on-demand treatment is used only at the time of a bleeding episode.

“The single greatest remaining challenge in the management of haemophilia is the development of inhibitors, often occurring in young patients, that can lead to more difficult to control and sometimes life-threatening bleeding,” said Bruce Ewenstein, M.D., Ph.D., vice president, clinical affairs in Baxter’s BioScience business. “The Pro-FEIBA investigator-initiated study is the first prospective, controlled clinical trial to evaluate the ability of FEIBA prophylaxis to reduce bleeding events, which is particularly encouraging given that there are limited treatment options available for these patients.”

The Prophylaxis with Factor Eight Inhibitor Bypassing Activity (Pro-FEIBA) study reported that patients with severe haemophilia A treated with FEIBA prophylactically during a six-month period experienced a 62 percent reduction in all bleeds in the prophylaxis period, an average of 5 bleeding events compared to an average of 13.1 during the on-demand treatment period. Sixty two percent of patients (16 of 26) were in the group that responded well to prophylaxis treatment, defined as those who had a greater than or equal to 50 percent reduction in overall bleeding, the target for success defined in the study protocol. In this “good responder group,” the overall reduction in bleeding rate was 84 percent. Thirty eight percent of patients (10 of 26) had a less than 50 percent reduction in bleeding events during the prophylactic period. In this group, bleeding was reduced by 28 percent. Two patients had an increase in bleeding events in the prophylaxis period.

Secondary outcome measurements were joint bleeding and target joint bleeding. During the prophylaxis period, patients experienced a 61 percent reduction in joint bleeding, an average of 4.2 joint bleeds versus an average of 10.8 during the on-demand treatment period. In target joints (those most prone to frequent bleeding, such as the elbow, knee and ankle), patients experienced a 72 percent reduction in bleeding. The number of patients with bleeding in target joints decreased from 18 to 11. Of those patients in the study achieving a reduction in bleeds, all were achieved with three doses of FEIBA (85 U/kg \pm 15 percent) per week.

One adverse event related to the study drug was an allergic reaction. Three patients (9 percent) had multiple events related to central venous access devices, including infection, bleeding, and line placement and removal.

A limitation of the study was its relatively short duration. While joint and other bleeding episodes were reduced during the six-month prophylaxis period, a longer, larger, parallel design trial is needed to determine if regular FEIBA infusions are a safe and effective treatment option for haemophilia A patients with inhibitors. In addition, the authors state it is not possible to draw

conclusions regarding relationships between patient age and the benefits of prophylaxis. A Baxter-sponsored clinical study, FEIBA PROOF, is evaluating the efficacy and safety of FEIBA prophylaxis compared to on-demand treatment in those living with haemophilia with high-titer inhibitors.

The Pro-FEIBA study was conducted by lead investigators Cindy Leissinger, M.D., from the Louisiana Center for Bleeding and Clotting Disorders, Tulane University Medical Center, New Orleans, USA, and Alessandro Gringeri, M.D., from the Department of Medicine and Medical Specialties, Fondazione IRCCS Cà Granda, Ospedale Maggiore Policlinico and Università degli Studi di Milano, Milan, Italy. The lead investigators oversaw all aspects of the study including design, data collection and analysis and manuscript development and submission. Baxter supplied the study drug (FEIBA) and provided a financial grant to support the study and authoring of the manuscript. The manuscript was subsequently revised by the authors who assumed responsibility for its accuracy and completeness.

About the Study Design

The objective of the investigator-initiated Pro-FEIBA study was to test if prophylaxis with FEIBA over a six-month period may be effective in preventing joint and other bleeds in severe haemophilia A patients with inhibitors compared to on-demand treatment. Following the initial six-month study period (with 12 patients receiving on-demand therapy and 14 receiving prophylaxis), each group crossed-over to the alternate treatment period for six months after a three-month wash-out period. The crossover design produced valid results with fewer patients than required for a parallel study design¹. Thirty-four patients were enrolled in the study, with 26 patients evaluated in the final analysis.

About Haemophilia A and Inhibitors

Haemophilia is a rare genetic blood clotting disorder that primarily affects males. People living with haemophilia do not have enough of, or are missing, one of the blood clotting proteins naturally found in blood. In people with haemophilia A, clotting factor VIII is not present in sufficient amounts or is absent. People with haemophilia do not bleed more profusely or faster than normal but bleed for a longer period of time.

Haemophilia is usually inherited, and about one in every 5,000 males is born with the disorder. About one third of new cases are caused by a new mutation of the gene in the mother or the child. In these cases, there is no previous history of haemophilia in the family. According to the World Federation of Hemophilia, more than 400,000 people in the world have haemophilia. All races and economic groups are affected equally.

Inhibitor development is considered one of the most serious adverse reactions associated with haemophilia treatment. Studies suggest this may occur in three out of every 10 people with severe hemophilia A. Inhibitors are antibodies that people with haemophilia can generate following exposure to blood clotting factor replacement therapy. These antibodies neutralize (inhibit) the action of clotting factor, which increases the risk of bleeding in people with inhibitors. Haemophilia patients with inhibitors have an increased risk of uncontrolled bleeding and bleeds are much more difficult to control compared to patients without inhibitors. Consequently, these patients can develop complications such as increased need for surgery and increased complexity of surgery.

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References

1. Louis TA, Lavori PW, Bailar JC, 3rd, Polansky M. Crossover and self-controlled designs in clinical research. N Engl J Med 1984;310:24-31.