SIPPET, an international randomized study, reports 87% higher incidence of inhibitors with recombinant factor VIII in patients with severehemophilia A

Results of the study have just been published in the May 26th issue of the New England Journal of Medicine

- **Results of the SIPPET (Survey of Inhibitors in Plasma-Products Exposed Toddlers) Study may have implications in the choice of products for treatment of patients with severe hemophilia A according to the principal investigators Flora Peyvandi and Pier Mannuccio Mannucci, from the Angelo Bianchi Bonomi Hemophilia and Thrombosis Center**

- **In particular, results show treatment of severe hemophilia A with recombinant factor VIII (rFVIII)is associated with an 87% higher incidence of inhibitors than treatment with plasma-derived factor VIII containing von Willebrand factor (pdFVIII/VWF) in previously untreated patients**

- **SIPPET is the first randomized controlled study on hemophilia and inhibitors that answers a key clinical question on the role of the Factor VIII product source. This investigator-initiated, multicenter clinical study involved 42 hemophilia treatment centers from all over the world**

- **The study was sponsored by theAngelo Bianchi Bonomi Foundation, withfinancial support from the Italian Ministry of Health and unrestricted grants from Grifols, Kedrion and LFB**

Milan (Italy), May 26th, 2016- SIPPET, a study which involved 42 centers in 14 countries in Europe, North and South America, Africa and Asia was designed to definitively settle the long-debated question whether factor VIII concentrates from different sources (plasma-derived containing VWFor recombinant technology) differ in risk of inhibitor development in previously untreated children (PUPs) with severe hemophilia A.

What makes SIPPET unique is that it is the first randomized study in which patients were randomly assigned to receive either plasma-derived FVIII/VWF or recombinant factor VIII concentrates. Randomized studies are considered by physicians to provide the highest level of evidence, since randomization minimizes confounding factors that could bias the outcome.

The study was conducted between 2010 and 2015. Of the 251 patients analyzed, 76 developed an inhibitor. Twenty-nine of the 125 patients in the plasma-derived arm and 47 of the 126 patients in the recombinant arm developed an inhibitor – the primary study endpoint. Cox regression analysis demonstrated that the treatment of PUPs with severe hemophilia A with recombinant factor VIII was associated with an 87% higher incidence of inhibitors than treatment with plasma-derived factor VIII/VWF. Similar results were found for the development of high-titre inhibitors.

The results, published in the May 26 issue of the New England Journal of Medicine, may have implications for the choice of productsto treatpatients, since the development of inhibitors remains the major challenge in the management of hemophiliaA.

SIPPET was an investigator-driven, international, multicenter, prospective, randomized, open label study, led by the investigators Flora Peyvandi and Pier Mannuccio Mannucci, from the Angelo Bianchi Bonomi Hemophilia and Thrombosis Center, Maggiore Policlinico Hospital and University of Milan (Italy). The study was sponsored by the Angelo Bianchi Bonomi Foundationand obtainedfinancial support from the Italian Ministry of Health and unrestricted grants from Grifols, Kedrion and LFB.

About hemophilia and inhibitors:

Hemophilia A patients suffer from lifelong risk of uncontrolled bleeding due to lack of clotting factor VIII. Bleeding can be treated or prevented by administration of factor VIII concentrates. Factor VIII can be made from donated human blood plasma, or by recombinant DNA technology. While these treatments have nearly normalized life expectancy in patients with hemophilia A, a substantial number of children develop antibodies (inhibitors) against factor VIII, thus complicating the benefits of treatment.The management of patients with inhibitors is both difficult and costly. The presence of inhibitors can lead to more difficult control of bleeding, as well as increased mortality. Additionally, the lifetime cost of managing a patient with hemophilia who develops an inhibitor can be extremely high.

Further information:

New England Journal of Medicine: http://www.nejm.org

SIPPET: http://www.sippet.org