Investor News

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Important step towards improved treatment for children with venous thromboembolism

Rivaroxaban demonstrates strong efficacy and safety profile in phase III study in children with thromboembolism

- Phase III EINSTEIN-Jr. study in children concludes the largest pediatric thromboembolism program delivering results consistent with those in adults
- Study shows a low risk of recurrent venous thromboembolism (VTE) in children treated with rivaroxaban compared with standard of care with low rates of bleeding
- First phase III data on the use of a non-vitamin K oral anticoagulant (NOAC) in a large pediatric population
- Study investigated a body weight-adjusted oral 20 mg equivalent dose of rivaroxaban for the prevention of recurrent VTE in children from birth to 17 years of age with confirmed VTE, including cerebral vein and sinus thrombosis

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Leverkusen, Germany, July 8, 2019 – Results from the phase III EINSTEIN-Jr. study showed a strong efficacy and safety profile of rivaroxaban in children with VTE, with results similar to those seen in previous studies in adults. Recurrent venous thromboembolism occurred at a low incidence with a numerical reduction of events in children treated with rivaroxaban compared with standard of care (heparins alone or in combination with a vitamin K antagonist such as warfarin). Major bleeding was not observed in the rivaroxaban group. Children received rivaroxaban as tablets or as a newly-developed suspension for oral use. The findings from EINSTEIN-Jr. were presented as a late breaker at the 27th International Society on Thrombosis and Haemostasis Congress (ISTH) in Melbourne, Australia today.

“Current treatment of VTE in children often relies on parenteral administration of anticoagulants and requires laboratory monitoring and dose adjustments. Up to now, pediatric anticoagulant treatment regimens were based mostly on observational data and on extrapolation of data obtained in adults. The EINSTEIN-Jr. study represents an

important step forwards for the treatment of VTE in children," said Professor Christoph Male, from the Department of Pediatrics, Medical University of Vienna in Austria.

The study showed that 4 out of 335 (1.2%) children treated with rivaroxaban and 5 out of 165 (3.0%) treated with standard of care had recurrent VTE. Furthermore, repeat imaging carried out at the end of the treatment period demonstrated an improved effect of rivaroxaban on thrombotic burden as compared with standard of care. Clinically relevant bleeding occurred in 10 children (3.0%; all were non-major bleeds) treated with rivaroxaban and in 3 children (1.9%; two were major bleeds and one was a non-major bleed) treated with standard of care.The absolute and relative safety and efficacy results seen in the EINSTEIN-Jr. study are consistent to those from previous rivaroxaban studies in adults.

"We have demonstrated that the use of the pediatric body weight-adjusted rivaroxaban regimens is efficacious and has shown positive safety results for the treatment of VTE in children," said Professor Male. "Availability of the rivaroxaban suspension for oral use will obviate the need for manipulations of adult dosage forms and substantially reduce the number of injections needed for standard anticoagulation treatment and blood sampling. The pediatric rivaroxaban regimen will represent an advantageous alternative treatment for children with VTE in the future. The data are consistent with the clinical outcomes observed in adult patients, as well as in other at risk subgroups of patients in the EINSTEIN program."

"Today, venous thromboembolism is being identified more often in childhood than in the past due to the increased survival of children with life-threatening or chronic medical conditions and also increased awareness of VTE among pediatricians," said Dr Joerg Moeller, Member of the Executive Committee at Bayer AG's Pharmaceuticals Division and Head of Research and Development. "The study results bring us one-step closer to providing pediatricians with a new therapeutic option for children. Rivaroxaban has the most extensive clinical study program of any non-vitamin K antagonist oral anticoagulant (NOAC) and we continue to investigate which patients will benefit most from use of this product."

Bayer will submit an application to the European Medicines Agency (EMA) for the extension of the Xarelto marketing authorization to make this new treatment option,

including the granules for oral suspension, available for children with venous thromboembolism.

VTE includes cerebral vein and sinus thrombosis, a blood clot in the brain, pulmonary embolism (PE), a blood clot that travels to the lung, and deep vein thrombosis (DVT), a blood clot in a deep vein (often in the legs). VTE is an increasingly common complication among hospitalized children with the most common risk factor for VTE being venous catheterization. Currently recommended treatment options for VTE include unfractionated heparin, low molecular weight heparin, fondaparinux with or without vitamin K antagonist therapy. No non-vitamin K oral anticoagulant is currently approved for use in this setting.

About the EINSTEIN-Jr. Study

The randomized, open-label phase III EINSTEIN-Jr. study included 500 children aged from birth to 17 years with documented acute VTE who had started heparin therapy. Children were assigned, in a 2:1 ratio, to receive body weight-adjusted rivaroxaban (tablets or suspension) in a 20 mg-equivalent dose, or standard of care with (low molecular weight) heparin or fondaparinux with or without vitamin K antagonist therapy. The main treatment period was 3 months, but children younger than 2 years with catheter-related VTE received 1 month of treatment. Repeat imaging was carried out at the end of the treatment period. Results were also interpreted in the context of previous studies evaluating rivaroxaban in adults with VTE.

Recurrent VTE occurred in 4 of the 335 (1.2%) children assigned to rivaroxaban and in 5 of the 165 (3.0%) children assigned to standard of care (hazard ratio, 0.40; 95% confidence intervals, 0.11 to 1.41). Repeat imaging showed an improved effect of rivaroxaban on thrombotic burden as compared with standard of care (P=0.012). Clinically relevant bleeding occurred in 10 children (3.0%; all non-major bleeds) with rivaroxaban and in 3 children (1.9%; two major and one non-major bleeds) with standard of care.

About Xarelto™

Rivaroxaban is the most broadly indicated non-vitamin K antagonist oral anticoagulant (NOAC) and is marketed under the brand name Xarelto™. Xarelto is approved for eight indications, protecting patients across more venous and arterial thromboembolic (VAT) conditions than any other NOAC:

- The prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation (AF) with one risk factor or more

- The treatment of pulmonary embolism (PE) in adults

- The treatment of deep vein thrombosis (DVT) in adults

- The prevention of recurrent PE and DVT in adults

- The prevention of venous thromboembolism (VTE) in adult patients undergoing elective hip replacement surgery

- The prevention of VTE in adult patients undergoing elective knee replacement surgery

- The prevention of atherothrombotic events (cardiovascular (CV) death, myocardial infarction (MI) or stroke) after an acute coronary syndrome in adult patients with elevated cardiac biomarkers and no prior stroke or transient ischemic attack (TIA) when co-administered with acetylsalicylic acid (ASA) alone or with ASA plus clopidogrel or ticlopidine

- The prevention of atherothrombotic events in adult patients with coronary artery disease (CAD) or symptomatic peripheral artery disease (PAD) at high risk for ischemic events when co-administered with acetylsalicylic acid

Xarelto is approved in more than 130 countries, whilst the approved labeling, including the number of indications may differ from country to country.

Rivaroxaban was discovered by Bayer, and is being jointly developed with Janssen Research & Development, LLC. Xarelto is marketed outside the U.S. by Bayer and in the U.S. by Janssen Pharmaceuticals, Inc. (Janssen Research & Development, LLC and Janssen Pharmaceuticals, Inc. are part of the Janssen Pharmaceutical Companies of Johnson & Johnson).

Anticoagulant medicines are potent therapies used to prevent or treat serious illnesses and potentially life-threatening conditions. Before initiating treatment with anticoagulant medicines, physicians should carefully assess the benefit and risk for the individual patient.

Responsible use of Xarelto is a very high priority for Bayer, and the company has developed a Prescribers Guide for physicians and a Xarelto Patient Card for patients to support best practice.

To learn more about thrombosis, please visit www.thrombosisadviser.com
To learn more about Xarelto, please visit www.xarelto.com

About Bayer
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References
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