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New Long-term Data Reinforce Safety Profile of Pradaxa® for Stroke Prevention in Atrial Fibrillation

New long-term data from the RELY-ABLE® study, the long-term extension of the pivotal RE-LY® trial of Pradaxa® (dabigatran etexilate) in patients with non-valvular atrial fibrillation (AF), were published online in *Circulation*,[1] the journal of the American Heart Association. Pradaxa® is the only treatment among the new generation of direct oral anticoagulants, which has been evaluated in a large set of AF patients for more than four years.[1] The long-term results reinforce the safety profile of Pradaxa®, which was originally established in the landmark RE-LY® trial.[1,2,3]

The new data from RELY-ABLE® contribute to the already available evidence supporting the safety profile of Pradaxa®. This evidence also includes the most recent analyses of real-world safety data from the US FDA Mini-Sentinel initiative[4] as well as assessments by other regulatory bodies, including the European Medicines Agency.[5]

"Before RELY-ABLE®, we already had data on the effects of two years of dabigatran etexilate treatment in patients with non valvular AF," said RELY-ABLE® lead investigator Professor Stuart Connolly, Director of the Division of Cardiology at McMaster University, Hamilton, Ontario. "The additional long-term data from RELY-ABLE® provide reassuring safety information for the long-term treatment of patients taking dabigatran etexilate."

The international multi-centre RELY-ABLE® trial was designed to evaluate the long-term safety of ongoing Pradaxa® therapy (110mg bid or 150mg bid) in patients with AF, following RE-LY®.[1] Patients enrolled in RELY-ABLE® continued Pradaxa® therapy for an additional 2.3 years in an ongoing blinded comparison, bringing the mean duration of treatment to 4.3 years. A total of 5,851 patients participated in the extension study.[1]

The unique results support the benefits of Pradaxa® over more than four years of long-term treatment. [1]

- During the additional 2.3 years of treatment following RE-LY®, rates of major events for both dabigatran 110 mg and 150 mg twice daily were consistent with those seen in RE-LY®
- There were no new safety findings identified during the additional observation period of RELY-ABLE®

Key results from RELY-ABLE® include:[1]

- Rates of major bleeding were 3.74 percent per year (n=238) and 2.99 percent per year (n=190) on Pradaxa® 150mg bid and 110mg bid respectively (HR = 1.26; 95% CI1.04-1.53)
- Very low rates of intracranial bleeding were sustained throughout the RELY-ABLE® study: 0.33 percent per year (n=21) and 0.25 percent per year (n=16) on Pradaxa® 150mg bid and 110mg bid respectively
- Incidence of haemorrhagic stroke was very low and similar between treatment arms: 0.13 percent per year (n=8) and 0.14 percent per year (n=9) on Pradaxa® 150mg bid and 110mg bid respectively

"We are pleased that the new long-term data from RELY-ABLE® add to the growing body of positive evidence for Pradaxa® in stroke prevention in atrial fibrillation. Pradaxa® is an important advancement in the treatment of patients with AF," commented Professor Klaus Dugi, Corporate Senior Vice President Medicine, Boehringer Ingelheim. "Boehringer Ingelheim is a science-based company that is proud to bring innovative products, like Pradaxa®, to patients and the medical community."

Additional findings from RELY-ABLE® include:[1]

- Rates of stroke or systemic embolism: 1.46 percent per year (n=93) and 1.60 percent per year (n=102) on Pradaxa® 150mg bid and 110mg bid respectively
- Rates of myocardial infarction were also low and similar between the two doses of Pradaxa® at 0.69 percent per year (n=44) and 0.72 percent per year (n=46) on Pradaxa® 150mg and 110mg, during the extended follow-up period.[1]

The efficacy and safety of Pradaxa® was established in the RE-LY® trial, one of the largest stroke prevention clinical studies ever conducted in patients with AF. Pradaxa® 150mg bid is the only novel oral anticoagulant, study of which has shown a significant reduction in the incidence of ischaemic strokes in patients with non-valvular AF compared to warfarin, offering a relative risk reduction of 25 percent.[2,3] Nine out of ten strokes are ischaemic strokes,[6] which can result in irreversible neurological injury with profound long-term consequences such as paralysis or inability to move one's limbs or formulate speech.[7]

Furthermore in RE-LY®, Pradaxa® 150mg bid provided a 36 percent reduction in the overall risk of stroke versus warfarin, demonstrating superior protection.[2,3] Pradaxa® 110mg bid was as effective as warfarin for the prevention of stroke and systemic embolism.[2,3] Both doses of Pradaxa® were associated with significantly lower total, intracranial and life-threatening bleeding compared to warfarin.[2,3] Pradaxa® 150mg bid showed a similar risk of major bleeds versus warfarin while Pradaxa® 110mg bid demonstrated a significantly lower risk.[2,3]

Pradaxa® is already widely approved for stroke prevention in atrial fibrillation and for primary prevention of VTE following total hip replacement or total knee replacement surgery.[8] Over 1.6 million patient years of experience in all licensed indications in over 100 countries support Pradaxa® as the leading novel oral anticoagulant.[9]

i RE-LY® was a PROBE trial (prospective, randomized, open-label with blinded endpoint evaluation), comparing two fixed doses of the oral direct thrombin inhibitor dabigatran etexilate (110mg bid and 150mg bid) each administered in a blinded manner, with open label warfarin.[2,3]

References:

1. Connolly SJ, et al. The Long Term Multi-Center Extension of Dabigatran Treatment in Patients with Atrial Fibrillation (RELY-ABLE) study. Circulation. 2013; published online before print June 14 2013, doi:10.1161/CIRCULATIONAHA.112.001139.
2. Connolly SJ, et al. Dabigatran versus warfarin in patients with atrial fibrillation. N Engl J Med. 2009;361:1139-51.
3. Connolly SJ, et al. Newly identified events in the RE-LY trial. N Engl J Med. 2010;363:1875-6.
4. Food and Drug Administration (FDA) Drug Safety Communication: Update on the risk for serious bleeding events with the anticoagulant Pradaxa. Viewed May 2013. Available at http://www.fda.gov/Drugs/DrugSafety/ucm326580.htm
5. European Medicines Agency's Committee for Medicinal Products for Human Use (CHMP) positive opinion on the renewal of the marketing authorisation for Pradaxa®. October 2012. Available at http://www.ema.europa.eu/docs/en_GB/document_library/Other/2012/10/WC500134406.pdf

6. Andersen KK, et al. Hemorrhagic and ischemic strokes compared: stroke severity, mortality, and risk factors. Stroke. 2009;40:2068–72.
7. NHLBI website. “What is Stroke?” Available at: http://www.nhlbi.nih.gov/health/health-topics/topics/stroke. Accessed on: October 10, 2012.
8. Pradaxa European Summary of Product Characteristics, 2013
9. Boehringer Ingelheim data on file.

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