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, 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. The long-term results reinforce the safety profile of Pradaxa®, which was originally established in the landmark RE-LY® trial.

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 as well as assessments by other regulatory bodies, including the European Medicines Agency.

"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®. 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.

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

- 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:

- 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% CI 1.04-1.53)
- 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:
- 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.

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. Nine out of ten strokes are ischaemic strokes, 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.

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

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. Over 1.6 million patient years of experience in all licensed indications in over 100 countries support Pradaxa® as the leading novel oral anticoagulant.

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.

References:
6. Andersen KK, et al. Hemorrhagic and ischemic strokes compared: stroke severity, mortality, and risk...


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