NAVIGATE ESUS

PHASE III

NAVIGATE ESUS will Provide Significant Insights into How Best to Protect Patients with a Recent Embolic Stroke of Undetermined Source (ESUS) from Recurrent Stroke

Phase III Rivaroxaban Superiority Study

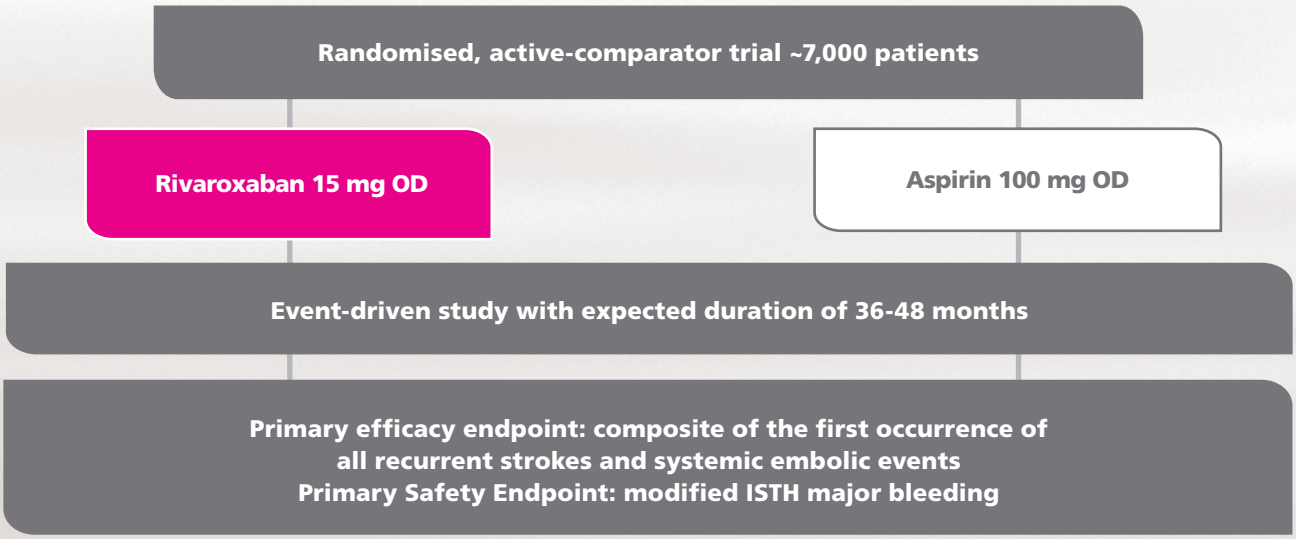
~7,000 Patients in >25 Countries

Collaboration between PHRI*, C-SPIN and Bayer**

ESUS accounts for about 25% of ischaemic strokes and approximately 300,000 people suffer from ESUS each year in North America and Europe[1]. Current Guidelines do not specifically comment on cryptogenic stroke or ESUS, but recommend antiplatelet therapy (aspirin, clopidogrel, aspirin + dipyridamole) for patients with non-cardioembolic stroke[2,3].

In the ROCKET AF study, once-daily rivaroxaban showed consistent safety and efficacy with a lower risk of intracranial hemorrhage compared with warfarin for both primary and secondary stroke prevention in patients with atrial fibrillation[4]. NAVIGATE ESUS will evaluate the potential benefit of once-daily rivaroxaban in secondary prevention of stroke in patients with a recent ESUS.

NAVIGATE ESUS Study Design



The extensive evaluation of rivaroxaban to protect different patient populations at risk of venous and arterial thromboembolism (VAT), makes it the most studied novel oral anticoagulant in the world. Rivaroxaban (Xarelto®) is already approved for five indications in seven areas of use and its investigation - both completed and ongoing - will include more than 275,000 patients in clinical trials and real world settings.

*Population Health Research Institute

**Canadian Stroke Prevention Intervention Network

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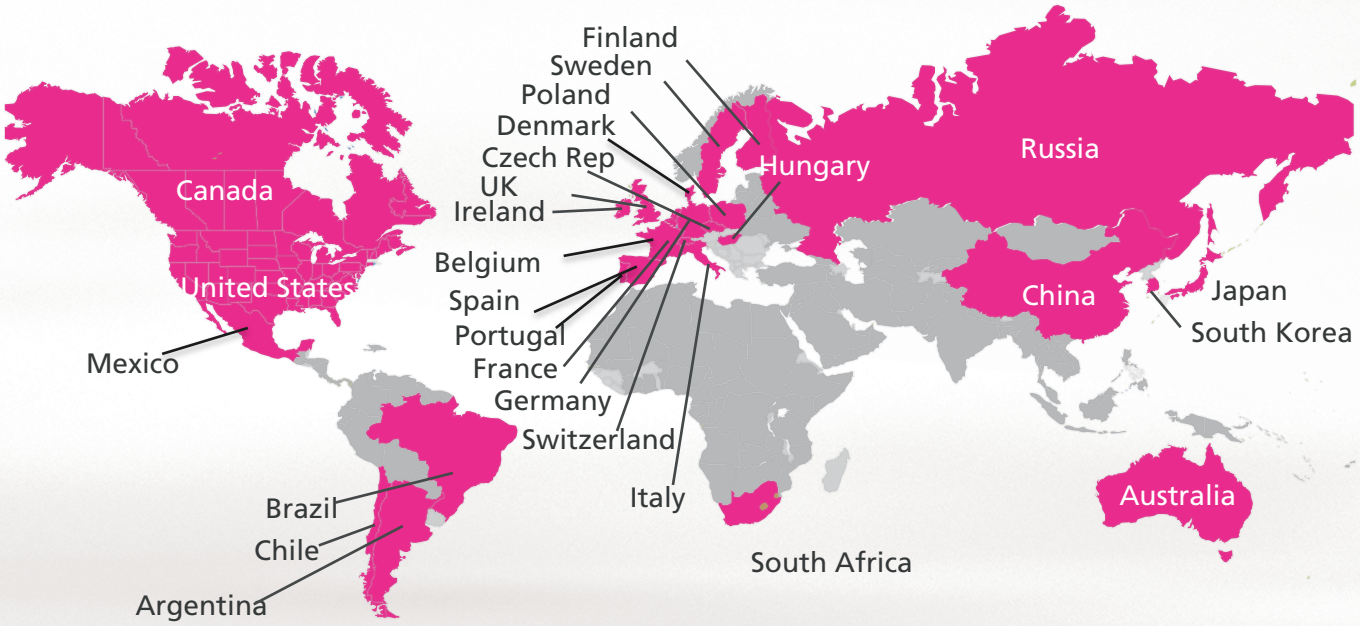
NAVIGATE ESUS Study Enrolling Patients from Around the World

Approximately 7,000 patients who have had a recent ESUS will be enrolled across 350 study sites in more than 27 countries



About Embolic Stroke of Undetermined Source (ESUS)

Every year, 15 million people worldwide suffer a stroke[5]; 85% are ischaemic with one quarter of these classified as ESUS[1,6]. For patients with ESUS, the origin of the blood clot that causes a stroke is unknown and cannot be identified with standard diagnostic procedures. ESUS patients have a 3-6% risk of secondary stroke per year on guideline-recommended antiplatelet(s)[1], showing a clear clinical need for further research in this area.

ESUS Compared to Cryptogenic Stroke

ESUS has previously been referred to as cryptogenic stroke after its cryptic origin. Approximately one in four ischaemic strokes without a clearly identified source have usually been termed cryptogenic. With the advance of imaging techniques and improved understanding of stroke pathophysiology, most cryptogenic strokes can now be identified as thromboembolic and thus related to blood clots. Therefore, focusing on the embolic nature of the stroke, even without conclusively determining the source in each and every patient offers a more clinically useful definition[1].

References

1) Hart RG, Diener HC, Coutts SB, et al. Embolic strokes of undetermined source: the case for a new clinical construct. Lancet Neurol. 2014: 13: 429–38. **2)** Albers GW, Amarenco P, Easton JD, et al. Antithrombotic and thrombolytic therapy for ischemic stroke (8th edn). Chest 2008: 133: 630s-669S. **3)** Adams RJ, Albers G, Alberts MJ, et al, and the American Heart Association, and the American Stroke Association. Update to the AHA/ASA. **4)** Patel MR, Mahaffey KW, Garg J, et al. Rivaroxaban versus warfarin in nonvalvular atrial fibrillation. N Engl J Med. 2011: 365(10): 883-891. **5)** World Heart Federation Stroke Factsheet. Available at: http://www.world-heart-federation.org/cardiovascular-health/stroke/. Accessed January 2015. **6)** Intercollegiate Stroke Working Party. National clinical guideline for stroke, 4th edition. London: Royal College of Physicians 2012