

Characterization of Patients with Embolic Strokes of Undetermined Source in the NAVIGATE ESUS Randomized Trial

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Background: The New Approach Rivaroxaban Inhibition of Factor Xa in a Global Trial vs. ASA to Prevent Embolism in Embolic Stroke of Undetermined Source (NAVIGATE-ESUS) trial is a randomized phase-III trial comparing rivaroxaban versus aspirin in patients with recent ESUS. **Aims:** We aimed to describe the baseline characteristics of this large ESUS cohort to explore relationships among key subgroups. **Methods:** We enrolled 7213 patients at 459 sites in 31 countries. Prespecified subgroups for primary safety and efficacy analyses included age, sex, race, global region, stroke or transient ischemic attack prior to qualifying event, time to randomization, hypertension, and diabetes mellitus. **Results:** Mean age was 66.9 ± 9.8 years; 24% were under 60 years. Older patients had more hypertension, coronary disease, and cancer. Strokes in older subjects were more frequently cortical and accompanied by radiographic evidence of prior infarction. Women comprised 38% of participants and were older than men. Patients from East Asia were oldest whereas those from Latin America were youngest. Patients in the Americas more frequently were on aspirin prior to the qualifying stroke. Acute cortical infarction was more common in the United States, Canada, and Western Europe, whereas prior radiographic infarctions were most common in East Asia. Approximately forty-five percent of subjects were enrolled within 30 days of the qualifying stroke, with earliest enrollments in Asia and Eastern Europe. **Conclusions:** NAVIGATE-ESUS is the largest randomized trial comparing antithrombotic strategies for secondary stroke prevention in patients with ESUS. The study population encompasses a broad array of patients across multiple continents and these subgroups provide ample opportunities for future research. **Key Words:** Stroke—cryptogenic stroke—cerebral embolism—Embolic Stroke of Undetermined Source (ESUS)—stroke prevention—rivaroxaban—aspirin—randomized trial.

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Introduction

Embolic stroke of undetermined source (ESUS) is a subset of cryptogenic stroke, and a diagnostic label proposed for an ischemic stroke that occurs without an identifiable and specifically treatable underlying stroke etiology, including greater than 50% stenosis in a large proximal artery in the territory of ischemia, atrial fibrillation or other

major-risk cardioembolic source, lacunar (small vessel occlusive) disease, or identified uncommon cause.¹ ESUS accounts for 15% to 30% of all ischemic strokes.² A wide range of potential cardiac, arterial, paradoxical, and hematological sources have been proposed that might be amenable to treatment with an anticoagulant.^{1,3,4} The New Approach Rivaroxaban Inhibition of Factor Xa in a Global trial vs. ASA to Prevent Embolism in Embolic Stroke of

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