

SOCRATES: Acute Stroke Or Transient Ischaemic Attack Treated with Aspirin or Ticagrelor and Patient Outcomes

Objective:

Primary objective

The primary objective of the study is to compare the effect of 90-day treatment with ticagrelor (180 mg [two 90 mg tablets] loading dose on Day 1 followed by 90 mg twice daily maintenance dose for the remainder of the study) vs aspirin (300 mg [three 100 mg tablets] loading dose on Day 1 followed by 100 mg once daily maintenance dose for the remainder of the study) for the prevention of major vascular events (composite of stroke, myocardial infarction [MI], and death) in patients with acute ischemic stroke or transient ischemic attack (TIA).

Secondary objectives

The first secondary objective of the study is to compare the effects of treatment with ticagrelor vs ASA for the prevention of subsequent ischemic stroke

Study Design:

This is a randomised, double-blind, double-dummy, international, parallel-group, multicentre study to assess the prevention of major vascular events (stroke, MI and death) with ticagrelor compared to ASA in patients with acute ischemic stroke or TIA.

Number of Subjects: Total sample size for the study is 9600 subjects.

Inclusion/Exclusion Criteria

Inclusion criteria

1. Provision of informed consent prior to any study specific procedures
2. Men or women ≥ 40 years of age
3. Either acute ischemic stroke or high-risk TIA as defined here and randomisation occurring within 24 hours after onset of symptoms:

Acute ischemic stroke, defined as:

- Neurological deficit attributed to the focal brain ischemia, **and** either of the following:
 - Persistent signs or symptoms of the ischemic event at the time of randomisation, OR
 - Acute, ischemic brain lesion documented by computed tomography scan or magnetic resonance imaging (diffusion-weighted imaging) within 24 hours of onset of symptoms
- National Institute of Health Stroke Score ≤ 5

High-risk TIA, defined as:

- Neurological deficit of acute onset attributed to focal ischemia of the brain by history or examination with complete resolution of the deficit, **and** at least one of the following:
 - ABCD₂ score ≥ 4 **and** TIA symptoms not limited to isolated numbness, isolated visual changes, or isolated dizziness/vertigo
 - Symptomatic intracranial arterial occlusive disease documented by transcranial doppler, ultrasound or vascular imaging, defined as at least 50% narrowing in diameter of a vessel that could account for the clinical presentation
 - Documented internal carotid arterial occlusive disease, defined as at least 50% narrowing in diameter of a vessel that could account for the clinical presentation

4. Head Computed Tomography (CT) or MRI ruling out hemorrhage or other pathology, such as vascular malformation, tumor, or abscess that could explain symptoms or contraindicate therapy

Exclusion criteria

1. Planned use of antithrombotic therapy in addition to study medication including antiplatelets (eg, open label ASA, GPIIb/IIIa inhibitors, clopidogrel, ticlopidine, prasugrel, dipyridamole, ozagrel, cilostazol) and anticoagulants (eg, warfarin, oral thrombin and factor Xa inhibitors, bivalirudin, hirudin, argatroban, unfractionated and low molecular weight heparins). In addition, patients receiving or requiring dual antiplatelet therapy with ASA and P2Y12 inhibitors will be excluded.
2. Known hypersensitivity to ticagrelor or ASA
3. Any history of atrial fibrillation, ventricular aneurysm or suspicion of cardioembolic pathology for TIA or stroke
4. Planned carotid, cerebrovascular, or coronary revascularization that requires halting study medication within 7 days of randomisation
5. Receipt of any intravenous or intra-arterial thrombolysis or mechanical thrombectomy within 24 hours prior to randomisation
6. Anticipated concomitant oral or intravenous therapy with strong cytochrome P450 3A (CYP3A) inhibitors or CYP3A substrates with narrow therapeutic indices that cannot be stopped for the course of the study
 - Strong inhibitors: ketoconazole, itraconazole, voriconazole, telithromycin, clarithromycin (but not erythromycin or azithromycin), nefazadone, ritonavir, saquinavir, nelfinavir, indinavir, atazanavir
 - CYP3A substrates with narrow therapeutic index: cyclosporine, quinidine, simvastatin at doses >40 mg daily or lovastatin at doses >40 mg daily
7. Anticipated requirement for long-term (>7 days) non-steroidal anti-inflammatory drugs (NSAIDs)
8. Patients with known bleeding diathesis or coagulation disorder (eg, thrombotic thrombocytopenic purpura)
9. History of previous symptomatic non-traumatic intracerebral bleed at any time (asymptomatic microbleeds do not qualify), gastrointestinal (GI) bleed within the past 6 months, or major surgery within 30 days
10. Known severe liver disease (eg, ascites or signs of coagulopathy)
11. Renal failure requiring dialysis
12. Pregnancy or lactation
13. Involvement in the planning and/or conduct of the study (applies to both AstraZeneca staff and/or staff at the study site)
14. Inability of the patient to understand and/or comply with study procedures and/or follow-up, in the opinion of the Investigator
15. Previous enrolment or randomisation in the present study
16. Participation in another clinical study with an investigational product during the last 30 days