ONLINE APPENDIX

Table S1. Inclusion criteria in the THALES study.

THALES inclusion criteria
1. Provision of signed informed consent prior to any study-specific procedure
2. ≥40 years of age
3. Acute onset of cerebral ischemia due to either: (a) AIS with NIHSS ≤5. AIS is defined as acute onset of neurological deficit attributed to focal brain ischemia, and either of the following: – Persistent signs or symptoms of the ischemic event at the time of randomization, OR – Acute ischemic brain lesion documented before randomization by CT scan or MRI (diffusion-weighted imaging) and that could account for the clinical presentation (b) 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: – $ABCD^2$ score ≥6 and TIA symptoms not limited to isolated numbness, isolated visual changes, or isolated dizziness/vertigo – Symptomatic intracranial arterial occlusive disease that could account for the clinical presentation, documented by transcranial Doppler or vascular imaging and defined as at least 50% narrowing in the diameter of the vessel lumen – Internal carotid arterial occlusive disease that could account for the clinical presentation, documented by Doppler, ultrasound, or vascular imaging, and defined as at least 50% narrowing in the diameter of the vessel lumen
4. Randomization occurring within 24 h after onset of symptoms; for wake-up strokes (when the time of symptom onset is not known), within 24 h from the time point at which the patient was reported to be in their normal condition
5. CT or MRI performed after symptom onset ruling out intracranial hemorrhage or other pathology, such as vascular malformation, tumor, or abscess that, according to the investigator could explain symptoms or contraindicate study treatment

$ABCD^2$ score is a clinical score based on: age, blood pressure, clinical features, duration of TIA, and diabetes.

AIS: acute ischemic stroke; CT: computed tomography; MRI: magnetic resonance imaging; NIHSS: National Institutes of Health Stroke Scale; TIA: transient ischemic attack.

Table S2. Exclusion criteria in the THALES study.

THALES exclusion criteria
1. Need for, or an anticipated need for, any of the following: (a) DAPT with aspirin and $P2Y_{12}$ inhibitors (including patients with carotid artery stenting and percutaneous coronary intervention) (b) Antiplatelets other than aspirin (e.g. GPIIb/IIIa inhibitors, clopidogrel, ticlopidine, prasugrel, dipyridamole, ozagrel, cilostazol, ticagrelor) and other antithrombotic agents with antiplatelet effects, including traditional/herbal medicine agents (c) Anticoagulants (e.g. warfarin, oral thrombin and factor Xa inhibitors, bivalirudin, hirudin, argatroban, fondaparinux, or unfractionated heparin and long-term treatment with low-molecular weight heparins). Short-term treatment ($\leq$7 days) with low-dose low-molecular weight heparin may be used in immobilized patients at the discretion of the investigator
2. Any history of atrial fibrillation/flutter, ventricular aneurysm, or suspicion of other cardioembolic pathology for TIA or stroke
3. Patients who should receive or have received any intravenous or intra-arterial thrombolysis or mechanical thrombectomy within 24 h prior to randomization
4. Planned carotid endarterectomy that requires halting investigational product within 3 days of randomization or is expected to require unblinding of investigational product (planned carotid endarterectomy is in itself not an exclusion criterion)
5. History of previous intracranial hemorrhage at any time (asymptomatic microbleeds do not qualify), gastrointestinal hemorrhage within the past 6 months, or major surgery within 30 days
6. Patients considered to be at risk of bradycardic events (e.g. known sick sinus syndrome or second- or third-degree atrioventricular block) unless already treated with a permanent pacemaker
7. Inability of the patient to understand and/or comply with study procedures and/or follow-up, in the opinion of the investigator
8. Known hypersensitivity to ticagrelor or aspirin
9. Need for or an anticipated need for oral or intravenous therapy with any of the following: (a) Strong CYP3A4 inhibitors (e.g. ketoconazole, clarithromycin [but not erythromycin or azithromycin], nefazodone, ritonavir, atazanavir) that cannot be stopped for the course of the study (b) Long-term ($>$7 days) non-steroidal anti-inflammatory drugs

10. Known bleeding diathesis or coagulation disorder (e.g. thrombotic thrombocytopenic purpura)
11. Known severe liver disease (e.g. ascites or signs of coagulopathy)
12. Renal failure requiring dialysis
13. Pregnancy or breastfeeding. Women of child-bearing potential who are not using a medically accepted method of contraception that is considered reliable in the judgment of the investigator
14. Involvement in the planning and/or conduct of the study (applies to both AstraZeneca staff and/or staff at the study site)
15. Previous enrollment or randomization in the present study
16. Participation in another clinical study with an investigational product at any time during the 30 days prior to randomization (regardless of when treatment with the investigational product was discontinued)

CYP3A4: cytochrome P450 3A; DAPT: dual antiplatelet therapy; GP: glycoprotein; TIA: transient ischemic attack.

Table S3. THALES national lead investigators.

Region/country	Lead investigators
Asia-Pacific	
Australia	Stephen Davis
China	Yongjun Wang
Hong Kong	Lawrence Wong
India	Padma Srivastava
	Sharma Vikram
Saudi Arabia	Fahmi Al-Senani
South Korea	Hee-Joon Bae
Taiwan	Tsong-Hai Lee
Thailand	Nijasri Charnnarong Suwanwela
Vietnam	Huy Thang Nguyen
North and South America	
Argentina	Sebastián Ameriso
Brazil	Luiz Marrone
Canada	Ken Butcher
Mexico	Antonio Arauz
Peru	Edwin Pretell
Europe	
Belgium	Robin Lemmens
Bulgaria	Ekaterina Titianova
Czech Republic	David Skoloudik
France	Pierre Amarenco
Germany	Joachim Röther
Hungary	Norbert Szegedi
Italy	Giancarlo Agnelli
	Danilo Toni
Poland	Anna Członkowska
Romania	Ovidiu-Alexandru Bajenaru
Russia	Lyudmila Stakhovskaya
Slovakia	Miroslav Brozman
Spain	Carlos Molina
Sweden	Lars Sjöblom
	Stefan James
Ukraine	Sergii Moskovko