Supplemental Table S1. Study Procedure of STRATEGY trial

Measures	Screening and randomization	Treatment period				
	1st visit	2nd visit	3rd visit	4th visit	5th visit	event follow-up
Time	baseline	24±2h	7±1d	at discharge	90 ±7d	
Eligibility	√					
Informed consent	√					
Demographics	√					
Medical history	√					
Physical examination	√	√	√		√	√
NIHSS	√	√	√		√	√
mRS	√				√	
EQ-5D					√	
Laboratory test	√ [1]	√ [2]				
Blood sample		√ [3]				
Radiographic evaluations[4]	√					
ECG	√					
Randomization	√					
Primary diagnosis	√					
Final diagnosis				√		
Drug dispense/Retrieve	√	√	√	√	√	√
Compliance	√	√	√	√	√	√
Endpoints		√	√	√	√	√
Evaluation of intracranial and extracranial arteries[5]				√		
Examination of cardiac structure and function[6]				√		
Radiographic reexamination[7]						√
High-resolution /7T MRI			√			
AE/SAEs		√	√	√	√	√

Concomitant medication	√	√	√	√	√	√

AE, adverse event; ECG, electrocardiograph; EQ-5D, EuroQol-5D; mRS, modified Rankin Scale; NIHSS, National Institute of Health Stroke Scale; SAE, Serious adverse event; TIA, Transient Ischemic Attack.

Notes：

1. The following laboratory tests must be completed during screening: complete blood count (CBC), hepatic function, renal function, blood coagulation function.
2. The following laboratory tests should be completed within 24h after randomization [including CBC, biochemical panel (including hepatic and renal function, blood lipids and creatine kinase), C-reaction protein, glycated hemoglobin, homocysteine, coagulation function].
3. Fasting venous blood samples should be collected within 24 hours after randomization (if not, 72 hours after randomization is the final deadline). Serum, plasma and leukocytes should be extracted and cryopreserved separately.
4. Radiographic evaluations, including brain MRI and MRA (or CTA), should be completed before randomization to observe cerebral infarction and parent artery. Brain MRI should be scanned at magnetic field intensity of at least 1.5 Tesla with slice thickness of 5 mm and slice gap of 6 mm. T1+T2+FLAIR+DWI/ADC sequences is necessary. T2* gradient echo (GRE-T2*) or susceptibility-weighted imaging (SWI) sequence is optional, depending on MRI devices of sub-centres. Baseline and follow-up imaging should be performed on the same device.
5. Evaluation of intracranial arteries includes any one of MRA, CTA, or DSA; evaluation of extracranial arteries includes any one of carotid artery ultrasound, CEMRA, supra-arch CTA and DSA. All the imaging data should be collected as DICOM (except for carotid artery ultrasound required to be photographed) form and uploaded.
6. Examination of cardiac structure and function includes cardiac ultrasonography and Holter.
7. Brain MR or CT should be finished when endpoint events occur to exam progressive stroke, recurrence of stroke or intracranial hemorrhage. Brain MRI (including T1+T2+FLAIR+DWI/ADC sequences) and MRA are the first choice.

Supplemental Table S2. Definitions of stroke events and vascular events

New-onset stroke	Acute symptoms and signs of neurologic defect caused by sudden abnormality of the blood supply. Damage of focal or whole brain, spinal or retinal vascular damage, which is related to cerebral circulation disorder. Both ischaemic stroke and haemorrhagic stroke are classified in this category.
Ischemic stroke	Definitions: (1) Symptoms or imaging evidence of acute newly onset focal neurologic deficit last for more than 24 hours after excluding other non-ischemic reasons, such as brain infection, head trauma, brain tumour, epilepsy, severe metabolic diseases, degeneration diseases or adverse effect of medications; or (2) Acute brain or retinal ischemic event with focal symptoms or signs lasts for less than 24 hours after excluding other causes with imaging evidence of new infarction; or (3) Progression of original vascular ischemic stroke (NIHSS increased ≥ 4 from baseline score after excluding haemorrhagic transformation or symptomatic intracerebral haemorrhage after cerebral infarction) lasts over 24 hours with new ischemic lesion on brain MRI or CT, which would be classified by TOAST aetiology standard.
Haemorrhagic stroke	Haemorrhagic stroke was defined as focal or whole brain or spine damage caused by non-traumatic bleeding into the brain parenchyma, intraventricular or subarachnoid.
Early neurological deterioration	The NIHSS score increasing by ≥ 2 points, or the score of hemiplegia increasing by ≥ 1 point, or the score of conscious disturbance increasing by ≥ 1 point compared with baseline within 7 days of onset. Intracranial haemorrhage can be determined by performing CT or MRI, and exacerbations not attributable to stroke such as cardiac, liver, and renal failure, among others are excluded.
Myocardial infarction	Third universal definition of myocardial infarction (Thygesen 2012) The term acute myocardial infarction (MI) should be used when there is evidence of myocardial necrosis in a clinical setting consistent with acute myocardial ischemia. Under these conditions any one of the following criteria meets the diagnosis for MI: 1. Detection of a rise and/or fall of cardiac biomarker values (preferably cardiac troponin [cTn]) with at least one value above the 99th percentile upper reference limit (URL) and with at least one of the following: (1) Symptoms of ischemia. (2) New or presumed new significant ST-segment–T wave (ST–T) changes or new left bundle branch block (LBBB). (3) Development of pathological Q waves in the ECG. (4) Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality. (5) Identification of an intracoronary thrombus by angiography or autopsy. 2. Cardiac death with symptoms suggestive of myocardial ischemia and

	presumed new ischemic ECG changes or new LBBB, but death occurred before cardiac biomarkers were obtained, or before cardiac biomarker values would be increased. 3. Percutaneous coronary intervention (PCI) related MI is arbitrarily defined by elevation of cTn values (>5×99th percentile URL) in patients with normal baseline values (≤99th percentile URL) or a rise of cTn values >20% if the baseline values are elevated and are stable or falling. In addition, either (1) symptoms suggestive of myocardial ischemia or (2) new ischemic ECG changes or (3) angiographic findings consistent with a procedural complication or (4) imaging demonstration of new loss of viable myocardium or new regional wall motion abnormality are required. 4. Stent thrombosis associated with MI when detected by coronary angiography or autopsy in the setting of myocardial ischemia and with a rise and/or fall of cardiac biomarker values with at least one value above the 99th percentile URL. 5. Coronary artery bypass grafting (CABG) related MI is arbitrarily defined by elevation of cardiac biomarker values (> 10 × 99th percentile URL) in patients with normal baseline cTn values (≤99th percentile URL). In addition, either (1) new pathological Q waves or new LBBB, or (2) angiographic documented new graft or new native coronary artery occlusion, or (3) imaging evidence of new loss of viable myocardium or new regional wall motion abnormality.
Vascular death	Vascular death include death due to stroke, cardiac sudden death, death caused by acute myocardial infarction, death caused by heart failure, death caused by pulmonary embolism, death caused by cardiac/cerebral interventions or operations (not caused by myocardial infarction) and death caused by other cardiovascular diseases. (Arrhythmia irrelevant to cardiac sudden death, rupture of aortic aneurysm or peripheral artery disease). Unexplained death happened within 30 days after stroke, myocardial infarction, or cardiovascular/cerebral vascular operation is considered as stroke, myocardial infarction and accidental death caused by operation separately.
Severe haemorrhage	Fatal, intracranial, or other haemorrhage causing substantial haemodynamic instability requiring intervention.
Moderate haemorrhage	Bleeding that requires blood transfusion but does not lead to hemodynamic instability requiring intervention.

Supplemental Table S3. Some studies of tirofiban applying on patients with ischaemic stroke

PMID	Patients	Sample size	Timing of medication	Dosage of medication	Other interventions	Bleeding events
36697890	acute LVO stroke	948	within 24 h of time from last known well	10 μg/kg within first 3 min followed by 0.15 μg/kg/min for up to 24h	endovascular thrombectomy after tirofiban, mono or dual antiplatelet therapy overlapped 4h with tirofiban	8% SICH
35943471	acute LVO stroke	945	within 24 h of time from last known well	10 μg/kg within first 3 min followed by 0.15 μg/kg/min for up to 24h	endovascular thrombectomy after tirofiban, mono or dual antiplatelet therapy overlapped 4h with tirofiban	9.7% SICH; 34.9% RICH
36481613	acute BAO stroke	645	within 122-410 min from onset	0.4 μg/kg/min for 30 min followed by 0.1 μg/kg/min for up to 24 h	endovascular treatment before or during tirofiban, mono or dual antiplatelet therapy after tirofiban	6.7% ICH; 4.8% SICH
36421943	anterior circulation occlusion with a defective thrombectomy	285	within 12h from onset	a bolus of 10 μg/kg followed by 0.13μg/kg/min for up to 24h	endovascular thrombectomy before tirofiban, dual antiplatelet after tirofiban	not associated with an increased risk of ICH, sICH
21852609	AIS	260	within 3-22h from onset	0.4 μg/kg/min for 30 min followed by 0.1 μg/kg/min for up to 48 h	standard antiplatelet therapy at the same time	30% ICH
34167477	AIS	255	within 24 h from onset	0.4 μg/kg/min for 30 min followed by 0.1 μg/kg/min	dual antiplatelet therapy after tirofiban	8% ICH

				for up to 48 h		
33274689	AIS	98	within 48 h from onset	0.4 μg/kg/min for 30 min followed by 0.1 μg/kg/min + 12500 U heparin per day for up to 48 h	dual antiplatelet therapy followed by mono antiplatelet therapy	No SICH
20090319	AIS	150	within 3-6h from onset	0.6 μg/kg/min for 30 min followed by 0.15 μg/kg/min for up to 72 h	N/A	11% ICH
29246609	AIS without arterial occlusion	50	within 4.5-24 h after onset	0.4 μg/kg/min for 30 min followed by 0.1 μg/kg/min for up to 24 h	mono antiplatelet therapy	No SICH; No ICH; No bleeding events
31570084	END within the first 24 h after IVT	187	within 24 h after onset	a bolus of 250-500μg followed by 4-8μg/min for 24 h	other antithrombotic therapy	5.8% ICH; 1.7% SICH
36461632	AIS with END, missing the IVT time window	123	within 24 h after admission	0.4 μg/kg/min for 30 min followed by 0.1 μg/kg/min for up to 48 h	mono or dual antiplatelet therapy	No SICH
19738371	progressive ischemic stroke (NIHSS+>2)	35	within 96 h after onset	0.4 μg/kg/min for 30 min followed by 0.1 μg/kg/min for up to 48 h	antithrombotic therapy at the same time	No ICH

AIS, acute ischaemic stroke; BAO, basilar artery occlusion; END, early neurological deterioration; ICH, intracranial hemorrhage; IVT, intravenous thrombolysis; LVO, large vessel occlusion; RICH, radiologic intracranial hemorrhage; SICH, symptomatic intracranial hemorrhage.