ForPatients
by Roche

Acute Ischemic StrokeThrombolysis

Tenecteplase in Stroke Patients Between 4 and 24 Hours

Tenecteplase in Stroke Patients Between 4.5 and 24 Hours

Trial Status	Trial Runs In	Trial Identifier
Completed	2 Countries	NCT03785678 ML40787

The information is taken directly from public registry websites such as ClinicalTrials.gov, EuClinicalTrials.eu, ISRCTN.com, etc., and has not been edited.

Official Title:

A Phase III, Prospective, Double-blind, Randomized, Placebo-controlled Trial of Thrombolysis in Imaging-eligible, Late-window Patients to Assess the Efficacy and Safety of Tenecteplase (TIMELESS)

Trial Summary:

This study will evaluate the efficacy and safety of tenecteplase compared with placebo in participants with acute ischemic stroke (AIS). All participants will receive standard-of-care therapy according to AmericanHeart Association/American Stroke Association clinical guidelines (2018). To determine eligibility for randomization, all participants will undergo multimodal CT or MRI at baseline. Only participants with a vessel occlusion (ICA or MCA M1/M2) and penumbral tissue will be randomized. The primary analysis is to compare the efficacy of tenecteplase versus placebo in all participants at Day 90.

Genentech, Inc.
Sponsor

Phase 3
Phase

NCT03785678 ML40787
Trial Identifiers

Eligibility Criteria:

Gender	Age	Healthy Volunteers
All	#18 Years	No

Inclusion Criteria:

- Patient/legally authorized representative has signed the Informed Consent Form
- Age >= 18 years

- AIS symptom onset within 4.5 to 24 hours Signs and symptoms consistent with the diagnosis of an acute anterior circulation ischemic stroke involving occlusion of the ICA, M1, or M2 vessels
- Functionally independent (mRS 0-2) prior to stroke onset
- Baseline NIHSS >=5 and that remains >=5 immediately prior to randomization
- Neuroimaging: ICA or M1, M2 occlusion (carotid occlusions can be cervical or intracranial, with or without tandem MCA lesions) by magnetic resonance angiography (MRA) or computed tomography angiography (CTA) AND target mismatch profile on CT perfusion or MR perfusion (ischemic core volume <70 mL, mismatch ratio is >=1.8 and mismatch volume is >= 15 mL)
- The mismatch volume is determined by FDA-approved imaging software in real time based on the difference between the ischemic core lesion volume and the Tmax>6s lesion volume. If both a CT perfusion and a multimodal MRI scan are performed prior to enrollment, the later of the 2 scans is assessed to determine eligibility. Only an intracranial MRA is required for patients screened with MRA; cervical MRA is not required. Cervical and intracranial CTA are typically obtained simultaneously in patients screened with CTA, but only the intracranial CTA is required for enrollment.

Alternative neuroimaging:

- If CTA (or MRA) is technically inadequate: Tmax>6s perfusion deficit consistent with an ICA or M1, M2 occlusion AND target mismatch profile (ischemic core volume <70 mL, mismatch ratio >= 1.8 and mismatch volume >= 15 mL as determined by RAPID software)
- If magnetic resonance perfusion (MRP) is technically inadequate: ICA or M1, M2 occlusion (carotid occlusions can be cervical or intracranial; with or without tandem MCA lesions) by MRA (or CTA, if MRA is technically inadequate and a CTA was performed within 60 minutes prior to the MRI) AND diffusion-weighted imaging (DWI) lesion volume <=25 mL for an M1 or ICA occlusion and =<15 mL for an M2 occlusion
- If CTP is technically inadequate: patient can be screened with MRI and randomized if neuroimaging criteria are met.
- Ability to comply with the study protocol, in the investigator's judgment

Exclusion Criteria:

General

- Current participation in another investigational drug or device study
- Active internal bleeding
- Known hypersensitivity or allergy to any ingredients of tenecteplase
- Known bleeding diathesis
- Known hereditary or acquired hemorrhagic diathesis, coagulation factor deficiency; recent oral anticoagulant therapy with INR >1.7
- Use of one of the new oral anticoagulants within the last 48 hours (dabigatran, rivaroxaban, apixaban, edoxaban)
- Pregnant
- Intracranial neoplasm (except small meningioma), arteriovenous malformation, or aneurysm
- Seizures at stroke onset if it precludes obtaining an accurate baseline NIHSS
- Severe, uncontrolled hypertension (systolic blood pressure >180 mmHg or diastolic blood pressure > 110 mmHg)
- For participants with suspected coagulopathy, platelet count must be checked prior to randomization and participant is excluded if baseline platelet count <100,000/microL
- Baseline blood glucose >400 mg/dL (22.20 mmol/L)
- Baseline blood glucose <50 mg/dL needs to be normalized prior to randomization
- Clot retrieval attempted using a neurothrombectomy device prior to randomization
- Intracranial or intraspinal surgery or trauma within 2 months

- Treatment with a thrombolytic within the last 3 months prior to randomization
- Other serious, advanced, or terminal illness (investigator judgment) with life expectancy less than 6 months
- Pre-existing medical, neurological, or psychiatric disease that would confound the neurological or functional evaluations
- History of cerebrovascular accident in the last 90 days
- Presumed septic embolus; suspicion of bacterial endocarditis
- Any other condition that, in the opinion of the investigator, precludes an endovascular procedure or poses a significant hazard to the patient if an endovascular procedure was to be performed

Imaging

- Unable to undergo a contrast brain perfusion scan with either MRI or CT
- Extensive early ischemic change (hypodensity) on non-contrast CT estimated to be >1/3 MCA territory, or significant hypodensity outside the Tmax>6s perfusion lesion that invalidates mismatch criteria (if patient is enrolled based on CT perfusion criteria)
- Significant mass effect
- Acute symptomatic arterial occlusions in more than one vascular territory confirmed on CTA/MRA (e.g., bilateral MCA occlusions, or an MCA and a basilar artery occlusion)
- Evidence of intracranial tumor (except small meningioma) acute intracranial hemorrhage, neoplasm, or arteriovenous malformation