Love at First Clot:

Can Tenecteplase Find Its Place Beyond the 4.5-Hour Window?

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Financial Disclosures

No conflicts of interest to disclose

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PollEv.com/sophierooks800

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Abbreviations

- **AA** – amino acid
- **ACA** – anterior cerebral artery
- **AIS** – acute ischemic stroke
- **aPTT** – activated partial thromboplastin time
- **AVM** – arteriovenous malformation
- **BOLO** – be on the look out
- **CT** – computed tomography
- **CTA** – computed tomography angiography
- **CTP** – computed tomography perfusion
- **CVA** – cerebrovascular accident
- **DBP** – diastolic blood pressure
- **DOAC** – direct oral anticoagulant
- **DWI** – diffusion-weighted magnetic resonance imaging
- **FLAIR** – fluid-attenuated inversion recovery sequence
- **h** – hour(s)
- **HTN** – hypertension
- **ICA** – internal carotid artery
- **INR** – international normalized ratio
- **IV** – intravenous
- **LVO** – large vessel occlusion
- **MCA** – middle cerebral artery
- **MI** – myocardial infarction
- **MRA** – magnetic resonance angiography
- **MRI** – magnetic resonance imaging
- **mRS** – modified Rankin scale
- **NCCT** – non-contrast computed tomography
- **NIHSS** – National Institutes of Health Stroke Scale
- **PCA** – posterior cerebral artery
- **PT** – prothrombin time
- **rtPA** – recombinant tissue plasminogen activator
- **SBP** – systolic blood pressure
- **sICH** – symptomatic intracranial hemorrhage
- **U.S.** – United States

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Pharmacist
Learning Objectives

Describe the clinical presentations of acute ischemic stroke based on the area of occlusion.

Compare the pharmacokinetic properties and safety profiles of alteplase and tenecteplase.

Evaluate the available literature surrounding the use of tenecteplase beyond the standard 4.5-hour window for acute ischemic stroke.

Given a patient case, assess a patient with acute ischemic stroke and determine if the use of tenecteplase is appropriate.

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Pharmacy Technician
Learning Objectives

List treatment options for acute ischemic stroke.

Differentiate between the administration techniques for alteplase and tenecteplase for acute ischemic stroke.

Recognize the risk versus benefit of using tenecteplase beyond the standard 4.5-hour window.

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Love Connection:
How Timing & Tenecteplase Meet

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Prevalence

Globally, stroke is the **second leading cause of death**

In the U.S., **every 40 seconds**, someone has a stroke; approximately **every 3 minutes**, someone dies

About **87%** of all strokes are **ischemic**

Currently **<10%** are eligible for fibrinolytic therapy due to **strict time constraints**

Stroke. 2023;54(8):1330-1339. ; Circulation. 2005;112(24_supplement). Centers for Disease Control and Prevention. October 24, 2024.

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Epidemiology

AGE	Can occur at any age, but **risk increases with age**
BIOLOGIC SEX	Female patients admitted with AIS have a **higher mortality rate** than males
RACE/ETHNICITY	Risk of stroke nearly **twice as high** for non-Hispanic Black adults as for White adults
SOCIO-ECONOMICS	Patients at or below the line of poverty at **greater risk of stroke**

Arch Med Sci Atheroscler Dis. 2021;6:e132-e134. ; MMWR Morbidity and Mortality Weekly Report. 2024;73(20):449-455. Centers for Disease Control and Prevention. October 24, 2024.

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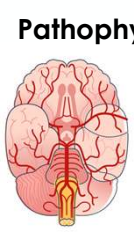
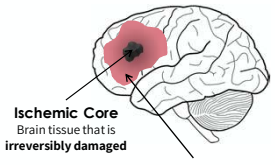
Pathophysiology





Ischemic Core
Brain tissue that is **irreversibly damaged**

Penumbra
Brain tissue that is **potentially salvageable**

Arterial Occlusion → ↓ Cerebral Blood Flow → ↓ O_2 & Glucose → ↑ Cell Membrane Alteration → ↑ Cell Death

Int J Mol Sci. 2020;21(20):7609. Trajectory Anatomy. 2024. ; DiPiro's Pharmacotherapy: A Pathophysiologic Approach, 12th Edition. McGraw Hill; 2023.

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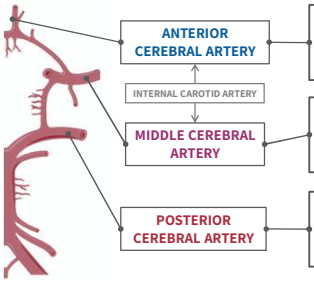
Clinical Presentation



ANTERIOR CEREBRAL ARTERY
Behavioral changes
Weakness: legs >> arms
Mild sensory defect

INTERNAL CAROTID ARTERY

MIDDLE CEREBRAL ARTERY
Weakness: face > arms > legs
Aphasia
Hemisensory defect (L or R)
Homonymous hemianopia

POSTERIOR CEREBRAL ARTERY
Confusion
Amnesia
Homonymous hemianopia
Visual agnosia

Comp Med. 2011;61(4):305-313.

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Current Treatment Algorithm
Pre-Hospital & Arrival

Activate Emergency Response (EMS)
Identify signs & symptoms of possible stroke

CRITICAL EMS ASSESSMENTS & ACTIONS
Establish time of symptom onset
Triage to nearest stroke center & alert hospital
Provide supportive care as needed

IMMEDIATE GENERAL ASSESSMENT AND STABILIZATION
Activate stroke team
Obtain IV access & perform laboratory assessments
Order emergent CT scan or MRI of brain
Obtain 12-lead ECG
Perform neurologic screening assessment (mRS preferred)

Stroke. 2019;50(12).

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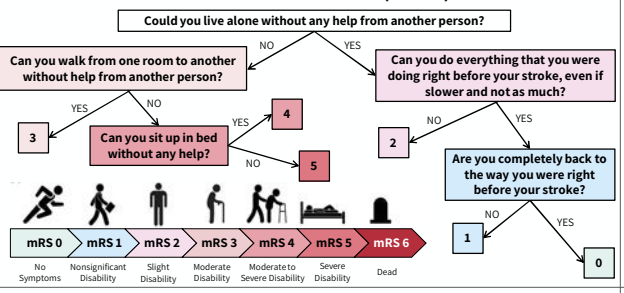
Modified Rankin Scale (mRS) *simplified



Stroke. 2011;42(8):2276-2279. 13

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Current Treatment Algorithm Pre-Hospital & Arrival

Activate Emergency Response (EMS)
Identify signs & symptoms of possible stroke

CRITICAL EMS ASSESSMENTS & ACTIONS
Establish time of symptom onset
Triage to nearest stroke center & alert hospital
Provide supportive care as needed

IMMEDIATE GENERAL ASSESSMENT AND STABILIZATION
Activate stroke team
Obtain IV access & perform laboratory assessments
Order emergent CT scan or MRI of brain
Obtain 12-lead ECG
Perform neurologic screening assessment (mRS preferred)

IMMEDIATE NEUROLOGIC ASSESSMENT BY STROKE TEAM OR DESIGNEE
Review patient history
Establish time of symptom onset or last known normal
Complete neurologic exam (NIHSS preferred)

Stroke. 2019;50(12). 14

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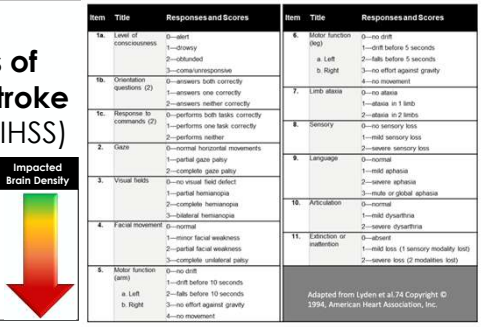
National Institutes of Health Stroke Scale (NIHSS)

NIHSS	Stroke Severity	Impacted Brain Density
0	No Stroke	
1 – 4	Mild Stroke	
5 – 15	Moderate Stroke	
16 – 20	Moderate to Severe Stroke	
21 – 42	Severe Stroke	



Stroke. 2017;48(2):513-519. 15

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Neuroimaging: Computed tomography (CT)

- **Non-contrast CT (NCCT):** most widely used first-line imaging tool in acute stroke
- Recommended as **initial mode of imaging** to assist in making decisions for IV rtPA

AIS Diagnosis

Clinical Presentation

Negative NCCT **- OR -** NCCT showing early ischemic changes

Stroke. 2019;50(12). Continuum (Minneap Minn). 2016;22(5, Neuroimaging):1399-1423. 16

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Neuroimaging: Magnetic resonance imaging (MRI)

Diffusion-weighted magnetic resonance imaging (DWI)

- Differentiate acute ischemia from stroke mimics
- Define infarct core
- Predict clinical neurologic outcome
- Predict final infarct volume

Fluid-Attenuated Inversion Recovery (FLAIR) sequence

- Reveal ischemic stroke as hyperintense area
- Useful for identifying acute strokes, especially when combined with DWI to assess time window for potential treatment with thrombolysis

Stroke. 2019;50(12). Cerebrovasc Dis. 2021;50(6):738-745. 17

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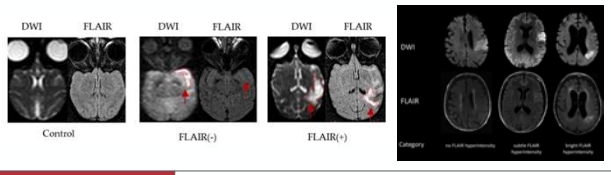
Neuroimaging: DWI-FLAIR Mismatch

- ❑ Situation where ischemic stroke appears clearly on DWI sequence but does not show corresponding signal change on FLAIR sequence
- ❑ Indicates recent stroke onset → potentially making the patient eligible for thrombolytic therapy within a specific time window



Stroke. 2022;53(5):1665-1673. 18

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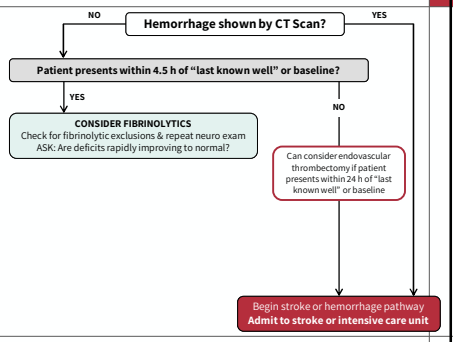
Current Treatment Algorithm Diagnosis & Treatment



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Fibrinolytic Eligibility

Inclusion Criteria

- Age ≥ 18 years
- Clinical diagnosis of ischemic stroke with neurologic deficit
- Time of symptom onset < 4.5 hours from treatment initiation

Use Clinical Judgement

- Unruptured/unsecured AVM or aneurysm > 10 mm
- Major surgery or non-head trauma
- History of bleeding diathesis
- Extensive hypoattenuation on initial CT scan

Exclusion Criteria

- History of intracranial hemorrhage or ischemic stroke (within 3 months)
- Symptoms/imaging suggesting subarachnoid or intracerebral hemorrhage
- Recent use of direct thrombin inhibitors or factor Xa inhibitors (within 48 hours)
- Use of treatment-dose low molecular weight heparin (within 24 hours)
- Infective endocarditis or intra-axial intracranial neoplasm
- Active internal bleeding or coagulopathy (e.g., platelets <100,000, INR>1.7, aPTT>40s, PT>15s)
- Severe head trauma (within 3 months)
- Gastrointestinal malignancy or bleeding (within 21 days)

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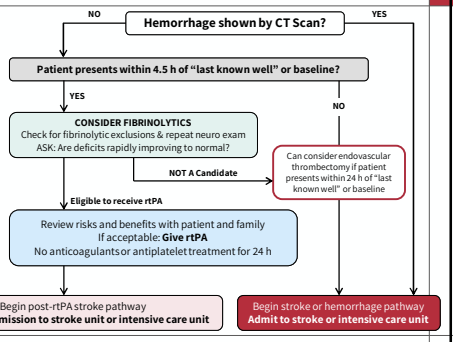
Current Treatment Algorithm Diagnosis & Treatment



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Pharmacotherapy: Overview

Acute Treatment of Ischemic Stroke – Antiplatelet Agents

Recommendation	Class (Strength) of Recommendation	Level (Quality) of Evidence
Aspirin 160-325 mg daily started within 48 hours of onset	I	A
Aspirin 81 mg daily and clopidogrel 75 mg daily for 21 days may be effective in reducing recurrent stroke in patients who do not receive IV alteplase and present with minor, non-cardioembolic stroke (NIHSS ≤3)	I	A

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Pharmacotherapy: Overview

Acute Treatment of Ischemic Stroke – IV Fibrinolytics

Recommendation	Class (Strength) of Recommendation	Level (Quality) of Evidence
Alteplase 0.9 mg/kg IV (maximum 90 mg) 10% as a bolus with the remainder given over 1 hour		
Within 3 hours of onset	I	A
Between 3 and 4.5 hours of onset	I	B-R
Tenecteplase 0.25 mg/kg IV bolus (maximum 25 mg) may be a reasonable alternative to alteplase for patients who are also eligible to undergo mechanical thrombectomy	IIb	B-R

European Stroke Organisation Recommendation

For patients who are eligible for intravenous thrombolysis, tenecteplase 0.25mg/kg can be used as a safe and effective alternative to alteplase 0.9 mg/kg

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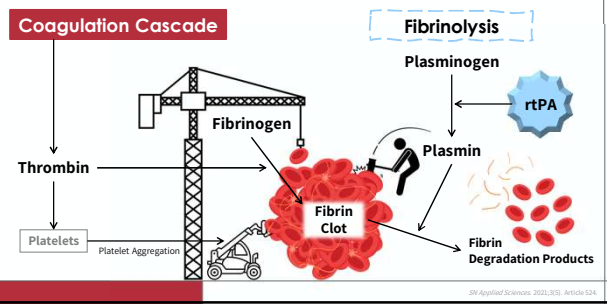
Pharmacotherapy: Fibrinolytics



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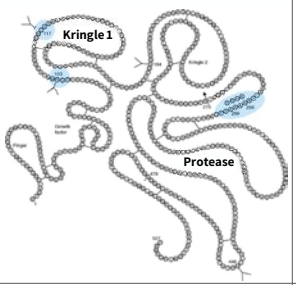
Pharmacotherapy: Alteplase vs. Tenecteplase

Agent	Alteplase	Tenecteplase
Structural modifications	-----	asparagine-117 → glutamate threonine-103 → asparagine AA 296-299 → tetra-alanine
Plasma half-life (min)	~ 5	~ 20
Clearance (mL/kg/min)	16.2	1.9
Fibrin specificity	++	+++
PAI-1 resistance	-	++
Thrombolytic potency	+	+++



The Lancet Neurology. 2024;23(11):1064-1065. 25

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Pharmacotherapy: Fibrinolytic Evolution

1995 — NINDS
Established initial time frame of alteplase administration within 3 hours of onset

2008 — ECASS III
Extended the time frame of alteplase administration to 4.5 hours of onset

2018 — EXTEND-IA TNK
Tenecteplase superior to alteplase when administered within 4.5 hours of onset

2019 — EXTEND
Attempted to extend the time frame of alteplase administration to 9 hours

Stroke. 2019;50(12). European Stroke Journal. 2023;8(1):8-54. 26

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Will You Accept This Rose?

What the Research Says About Expanding the 4.5-Hour Window

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Intravenous Tenecteplase for Acute Ischemic Stroke Within 4.5–24 Hours of Onset (ROSE-TNK)

Journal of Stroke. 2023;25(3):371-377.

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Study Objective & Design

- ❑ To determine the effect of intravenous tenecteplase for acute ischemic stroke within 4.5 to 24 hours of onset

Phase II

Randomized | Investigator-initiated | Multicenter | Blinded endpoints

Journal of Stroke. 2023;25(3):371-377. 29

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Inclusion Criteria

- Acute ischemic stroke **confirmed by CT or MRI**
- First stroke onset or past stroke without obvious neurological deficit **(mRS≤1)**
- **NIHSS Score: 6-25**
  - or NIHSS score ≤ 5 but responsible vessel occlusion or severe stenosis on CTA/MRA
- **Patient Age:** 18 – 80
- **The time from onset to treatment:** 4.5 - 24 h
- **Imaging Requirements:**
  - DWI infarct region: no more than 1/3 of MCA territory or 1/2 of ACA territory or 1/2 of PCA territory
  - DWI infarct volume <70 mL
  - Presence of DWI/FLAIR mismatch

Journal of Stroke. 2023;25(3):371-377. 30

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Exclusion Criteria

- Planned endovascular treatment
- Serious neurological deficits before onset (mRS ≥ 2)
- SBP ≥185 mmHg or DPB ≥110 mmHg
- Blood glucose < 50 mg/dL
- Oral warfarin is being taken and INR >1.6 or aPTT abnormal
- MI within 3 months
- Intracranial or spinal cord surgery within 3 months
- Major surgery within 1 month

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Interventions

TNK

Intravenous tenecteplase 0.25 mg/kg (max dose: 25 mg) administered as a single IV bolus

Control

Standard Medical Treatment

- Antiplatelets, statins, blood pressure, & glucose control

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Endpoints

Primary Endpoint

- Excellent functional outcome (90-day mRS scores 0–1)

Safety Endpoints

- sICH within 48 h
- Any bleeding events within 7 days
- Death within 14 days

Secondary Endpoints

- Favorable functional outcomes (90-day mRS scores 0–2)
- Change in NIHSS score from baseline to 24 h after randomization
- Change in NIHSS score from baseline to 7 days after randomization
- Early neurological improvement

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Statistical Analysis

Unadjusted Intention to Treat Analysis

Categorical Data	Continuous Data	
Chi-square test	Rank Sum test	T-test

Covariate-adjusted binary logistic regression analyses performed for all outcomes, adjusting for 6 pre-specified prognostic factors

- Age
- Sex
- SBP
- Previous ischemic stroke
- NIHSS at presentation
- Time from onset to randomization

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Study Sample

Sample Size: 80 patients from 14 hospitals in China

TNK	Standard Medical Treatment
n = 40	n = 40

Median time from symptom onset to treatment: **~ 12 h**

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Baseline Characteristics

Characteristic	TNK	Standard Medical Treatment
Median Age	63 years	63 years
Male Sex	77.5%	65%
Hypertension	60%	70%
Diabetes	22.5%	32.5%
Current Smoker	47.5%	52.5%
Previous Ischemic Stroke	27.5%	30%
Admission NIHSS score	7.5	7
Large vessel occlusion	42.5%	45%
Wake up stroke	60%	57.5%

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Results

Outcome	TNK	Standard Medical Treatment	Adjusted OR (95% CI)	P-value
Primary Outcome				
Excellent functional outcome	52.5%	50%	1.10 (0.41-2.97)	0.85
Secondary Outcomes				
Favorable functional outcomes	65%	60%	1.44 (0.49-4.22)	0.50
Change in NIHSS score at 24 h	-2	0	-1.11 (-2.49-0.26)	0.11
Change in NIHSS score at 7 days	-3	-2	-0.21 (-1.67-1.26)	0.78
Early neurological improvement	27.5%	7.5%	5.00 (1.16-21.50)	0.03
Safety Outcomes				
sICH within 48 h	0	0		
Any bleeding events within 7 days	0	0		
Death within 14 days	0	0		

NO LOVE LOST

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Critique

Limitations

- Open-label design
- Small sample size
- Solely reflective of Chinese ethnicity
- Population not representative of patients within an extended time window

Strengths

- Randomized, multicenter design
- Blinded endpoint evaluations

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Interpretation

When compared to standard medical treatment, TNK administered between 4.5 to 24 h after stoke onset

- Showed improved early neurologic outcomes
- Did not present a significant safety risk

TNK may be a safe option for patients with AIS who present within the 4.5-to-24-hour window after "last-known-well"

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Tenecteplase for Ischemic Stroke at 4.5 to 24 Hours without Thrombectomy (TRACE-III)

New England Journal of Medicine. 2024;391(3):203-212.

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Study Objective & Design

❑ To investigate the efficacy and safety of TNK administered 4.5 to 24 h after stroke onset in patients with salvageable tissue and no access to endovascular thrombectomy

Phase III

Multicenter | Randomized | Open-label | Blinded-endpoints

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Inclusion Criteria

Internal carotid artery, middle cerebral artery (M1 or M2) occlusion **confirmed by CTA/MRA**

Pre-stroke **mRS≤1**

NIHSS Score

Baseline: 6 – 25

Patient Age: ≥ 18

The time from onset to treatment: 4.5 - 24 h (including wake-up stroke & unwitnessed stroke)

Imaging Requirements:

- Target mismatch profile on CTP or MRI+MR perfusion
- Ischemic core volume < 70mL, mismatch ratio ≥ 1.8, and mismatch volume ≥ 15mL identified by validated automated evaluation software

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Exclusion Criteria

- Anticipated endovascular treatment
- SBP ≥180 mmHg or DBP ≥100 mmHg
- Any known impairment in coagulation
- Blood glucose > 400 mg/dL OR < 50 mg/dL
- Hypodensity in >1/3 MCA territory on NCCT
- Intracranial hemorrhage or ischemic stroke within 3 months
- Multiple arterial occlusion
- Acute or past ICH identified by CT or MRI

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Interventions

TNK

Intravenous tenecteplase 0.25 mg/kg (max dose: 25 mg) administered as a single IV bolus

Control

Standard Medical Treatment

- Aspirin 100 mg combined with clopidogrel 75 mg, aspirin 100 mg alone, or clopidogrel 75 mg alone

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Endpoints

Primary Endpoint

- Absence of disability (90-day mRS scores 0–1)

Safety Endpoints

- sICH within 36 h
- Death from any cause within 90 days
- Moderate or severe systemic bleeding within 90 days
- Any adverse events within 90 days

Secondary Endpoints

- Functional independence (90-day mRS scores ≤ 2)
- Major neurologic improvement at 72 h after treatment (defined as a reduction from baseline of ≥8 points on the NIHSS or an NIHSS score of ≤1)
- Reperfusion at 24 h after treatment
- Change from baseline in NIHSS score at 7 days

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Statistical Analysis

Unadjusted Intention to Treat Analysis

Categorical Data		Continuous Data	
Chi-square test	Fisher's Exact test	Rank Sum test	T-test

Logistic regression analyses performed for the primary efficacy outcome, adjusting for 6 pre-specified factors

- Age
- HTN
- Diabetes
- Site of LVO
- NIHSS at presentation
- Onset-to-treatment time

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Study Sample

Sample Size: 516 patients from 58 centers in China

TNK	Standard Medical Treatment
n = 264	n = 252

Median time from symptom onset to treatment: **~ 12.4 h**

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Baseline Characteristics

Characteristic	TNK	Standard Medical Treatment
Median Age	67 years	68 years
Male Sex	69.3%	66.3%
Hypertension	67%	71.4%
Diabetes	26.1%	28.2%
Atrial Fibrillation	18.6%	19%
Median NIHSS score	11	10
Baseline mRS score of 1	87.1%	85.7%
Baseline mRS score of 0	12.9%	14.3%
Known onset of stroke time	54.2%	59.1%
Wake up stroke	38.3%	33.3%

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Results

Outcome	TNK	Standard Medical Treatment	Effect Size (95% CI)	NNT
Primary Outcome				
Absence of disability	33%	24.2%	1.37 (1.04-1.81) p = 0.03	12
Secondary Outcomes				
Functional independence at 90 days	43.6%	33.3%	1.31 (1.05-1.63)	10
Major neurologic improvement at 72 h after treatment	16%	6%	2.66 (1.51-4.69)	10
Reperfusion at 24 h after treatment	20.1%	11.8%	1.70 (1.10-2.64)	12
Change from baseline in the NIHSS score at 7 days	-4	-2	-1.47 (-2.30 - -0.64)	

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Results

Outcome	TNK	Standard Medical Treatment	Effect Size (95% CI)
Safety Outcomes			
sICH within 36 h after randomization	3%	0.8%	3.82 (0.82-17.87)
Death from any cause within 90 days	35%	33%	1.01 (0.65-1.58)
Moderate or severe systemic bleeding within 90 days	1.9%	0.8%	2.36 (0.46-12.09)
Any adverse event	50.8%	51.2%	0.99 (0.84-1.17)

NO LOVE LOST

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Results – Subgroup Analysis

Relative Rate of a mRS Score of 0 or 1 at 90 Days (control vs. tenecteplase)

Overall	24.2% vs. 33% [95% CI, 1.37 (1.04–1.81)]
Male Sex	25.8% vs. 36.6% [95% CI, 1.42 (1.03–1.95)]
Time from symptom onset to treatment > 9 to 24 h	25.4% vs. 36.5% [95% CI, 1.44 (0.96–2.17)]
MCA Occlusion	**M1:** 23.1% vs. 32.8% [95% CI, 1.43 (0.95–2.15)] **M2:** 21.1% vs. 39.7% [95% CI, 1.89 (0.94–3.82)]

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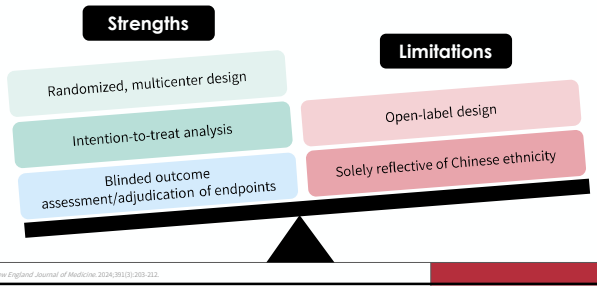
Critique



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Interpretation

When compared to standard medical treatment, tenecteplase administered between 4.5 to 24 hours after stoke onset

- Improved disability-free recovery
- Did not present significant safety risk

Tenecteplase may be a safe and efficacious treatment option for patients suffering from acute ischemic stroke due to large vessel occlusion within 4.5-to-24-hour window after "last-known-well" in facilities that do not have thrombectomy capabilities

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Tenecteplase for Stroke at 4.5 to 24 Hours with Perfusion-Imaging Selection (TIMELESS)

New England Journal of Medicine. 2024;390(8):701-711.

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Study Objective & Design

- To test if intravenous tenecteplase, given 4.5 to 24 hours after stroke onset, benefits patients with large-vessel occlusion and salvageable ischemic brain tissue

Phase III

Multicenter | Double-blind | Randomized | Placebo-controlled

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Inclusion Criteria

- Acute ischemic stroke **confirmed by CT or MRI**
- Functionally independent prior to stroke onset **(mRS≤2)**
- **NIHSS Score: ≥ 5**
  - Remains ≥5 immediately prior to randomization
- **Patient Age:** ≥ 18
- **The time from onset to treatment:** 4.5 - 24 h (including wake-up stroke)
- **Imaging Requirements:**
  - ICA or M1, M2 occlusion (carotid occlusions can be cervical or intracranial, with or without tandem MCA lesions) by MRA or CTA
  - **AND**
  - Target mismatch profile on CT perfusion or MRI (ischemic core volume <70 mL, mismatch ratio is >1.8 and mismatch volume is >15 mL)

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Exclusion Criteria

- Planned endovascular treatment
- SBP ≥185 mmHg or DBP ≥110 mmHg
- Blood glucose > 400 mg/dL OR < 50 mg/dL
- Treatment with a thrombolytic ≤ 3 months
- Active internal, subarachnoid, or intracranial hemorrhage
- PMH of intracranial hemorrhage or tumor
- Use of a DOAC within 48 hours
- Previous CVA within 90 days

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Interventions

TNK

Intravenous tenecteplase 0.25 mg/kg (max dose: 25 mg) administered as IV bolus

Control

Placebo administered as IV bolus

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Endpoints

Primary Endpoint

- Ordinal mRS score at day 90

Safety Endpoints

- sICH within 36 h
- Death within 30 days
- Death within 90 days

Secondary Endpoints

- Functional independence (90-day mRS scores 0 – 2)
- Recanalization of implicated vessel at 24 h
- Reperfusion at 24 h after randomization

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Statistica

NOTICE

- **Data management** and site monitoring was overseen by **Genentech**
- **Data analysis** was performed by two authors who are employees of **Genentech**

The prima… | …b-groups | Age | Occlusio… | Location | Size | …m …o …nt | Time to arterial puncture

60

Study Sample

Sample Size

458 patients at 108 centers in U.S. and at 4 centers in Canada

TNK	Placebo
n = 228	n = 230

Median time from symptom onset to treatment: **~ 13 h**

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Baseline Characteristics

Characteristic	TNK	Placebo
Median Age	72 years	73 years
Female Sex	53.5%	53.5%
Caucasian	74.1%	73.9%
Median NIHSS score	12	12
Occlusion Site: M1 Segment	48.2%	50.9%
Occlusion Site: M2 Segment	39%	36.5%
Endovascular Thrombectomy Performed	77.2%	77.4%

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Results

Outcome	TNK (n = 228)	Placebo (n = 230)	Adjusted OR (95% CI)	P-value
Primary Efficacy Outcome				
Median mRS score at 90 days	3	3	1.13 (0.82–1.57)	0.45
Secondary Efficacy Outcomes				
Functional independence at day 90	46%	42.4%	1.18 (0.80–1.74)	
Recanalization at 24 h	76.7%	63.9%	1.89 (1.21–2.95)	
Reperfusion at 24 h	56.9%	57.7%	1.04 (0.69–1.57)	
Safety Outcomes				
Death within 30 days	14.7%	15%		
Death within 90 days	19.7%	18.2%		
sICH within 36 h	3.2%	2.3%		

NO LOVE LOST

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Results – Subgroup Analysis

Median mRS score at 90 days (adjusted common odds ratio)

Overall	95% CI, 1.13 (0.82–1.57)
Time from symptom onset to treatment < 16 h	95% CI, 0.94 (0.65–1.37)
Endovascular thrombectomy performed	95% CI, 1.18 (0.81–1.70)
MCA Occlusion	**M1:** 95% CI, 1.59 (1.00–2.52) **M2:** 95% CI, 0.76 (0.45–1.30)

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Critique

Strengths	Limitations
Double-blind	Sponsor bias
Randomized, multicenter design	Evaluation of multifaceted intervention
Intention-to-treat analysis	Underrepresentation of non-Caucasian ethnic/racial groups
Adequately powered	Unclear percentage of population with wake-up stroke

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Interpretation

When compared to placebo, tenecteplase initiated 4.5 to 24 hours after stroke onset

- Did not provide benefit to patients
- Did not cause harm to patients or present significant safety risk

Tenecteplase may be a safe option for patients who present within 4.5-to-24-hour window after "last-known-well" who have access to endovascular thrombectomy

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Baseline Characteristics Comparison

	ROSE-TNK		TRACE-III		TIMELESS	
	TNK	Standard Medical Therapy	TNK	Standard Medical Therapy	TNK	Placebo
Median age	63 years	63 years	67 years	68 years	72 years	73 years
Median NIHSS on admission	7.5	7	11	10	12	12
Median time from symptom onset to treatment	11.47 h ± 4.70 h	12.52 h ± 4.68 h	12.4 h [8.8–16.3 h]	12.8 h [9.0–17.5 h]	12.3 h [9.2–15.6 h]	12.7 h [8.7–16.5 h]

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Study Results Comparison

	ROSE-TNK		TRACE-III		TIMELESS	
	TNK	Standard Medical Therapy	TNK	Standard Medical Therapy	TNK	Placebo
90-day mRS scores 0–1						
90-day mRS scores 0–2						
sICH within 36 hours						

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The Final Rose:
What's Next for Stroke Treatment with Tenecteplase?

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Extended Window Treatment Algorithm
Pre-Hospital & Arrival

Activate Emergency Response (EMS)
Identify signs & symptoms of possible stroke

CRITICAL EMS ASSESSMENTS & ACTIONS
Establish time of symptom onset
Triage to nearest stroke center & alert hospital
Provide supportive care as needed

IMMEDIATE GENERAL ASSESSMENT AND STABILIZATION
Activate stroke team
Obtain IV access & perform laboratory assessments
Order emergent CT scan or MRI of brain
Obtain 12-lead ECG
Perform neurologic screening assessment (mRS preferred)

IMMEDIATE NEUROLOGIC ASSESSMENT BY STROKE TEAM OR DESIGNEE
Review patient history
Establish time of symptom onset or last known normal
Complete neurologic exam (NIHSS preferred)

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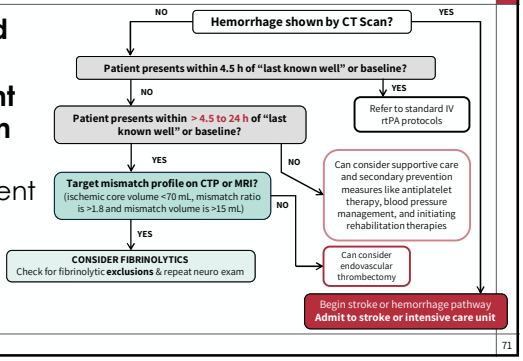
Extended Window Treatment Algorithm
Diagnosis & Treatment



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Extended Window Treatment
Inclusion & Exclusion Criteria

Inclusion Criteria
- Age ≥18 years
- Acute ischemic stroke confirmed by CT or MRI
- The time from onset to treatment: 4.5 - 24 h
- Functionally independent prior to stroke onset (mRS≤2)
- NIHSS Score: 6-25
- Target mismatch profile on CT perfusion or MRI (ischemic core volume <70 mL, mismatch ratio is >1.8 and mismatch volume is >15 mL)

Exclusion Criteria
- SBP ≥185 mmHg or DBP ≥110 mmHg
- Blood glucose > 400 mg/dL OR < 50 mg/dL
- Multiple arterial occlusion
- History of intracranial hemorrhage or ischemic stroke (within 3 months)
- Symptoms/imaging suggesting subarachnoid or
- Pregnant or currently lactating

Important Note:
Trial cut-off time: **24 h**
Most patients included were within **8 – 18 h** of their "last known well"

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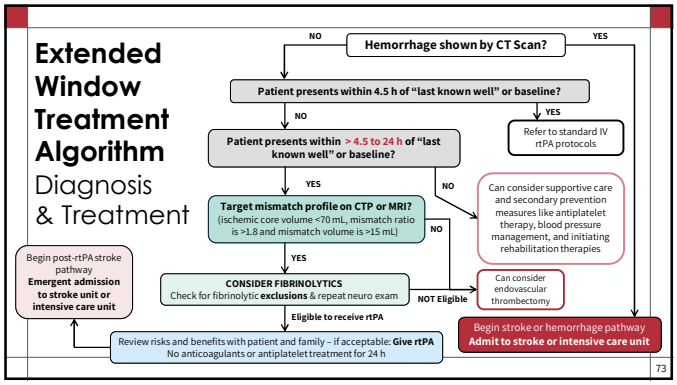

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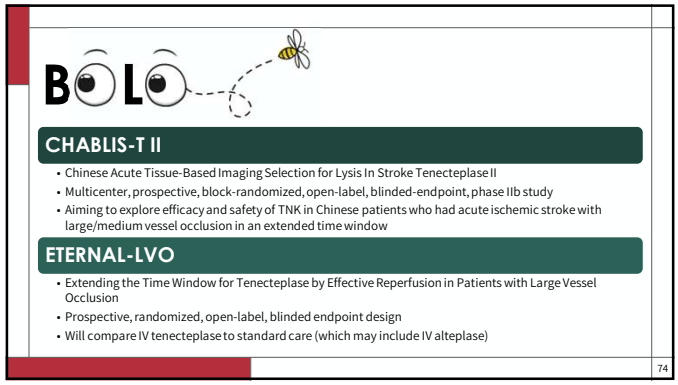

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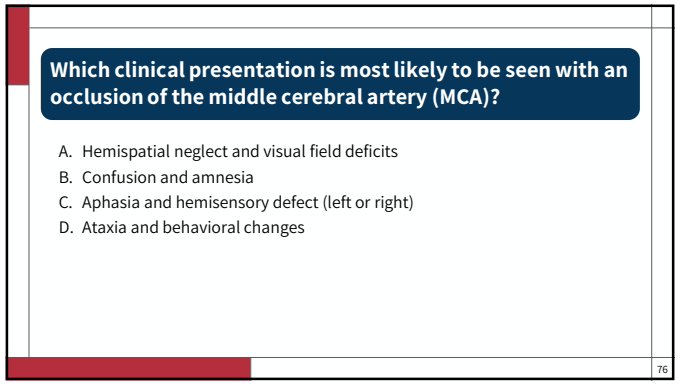

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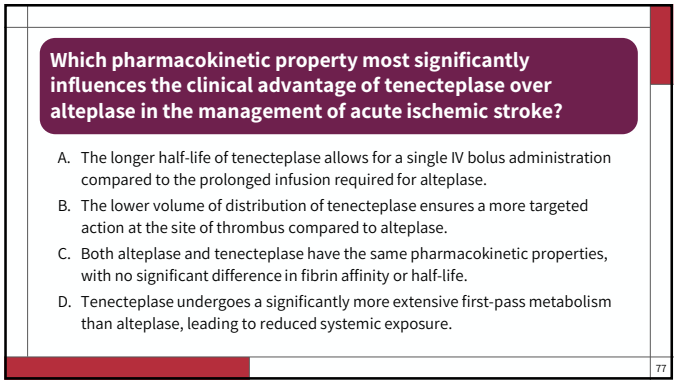

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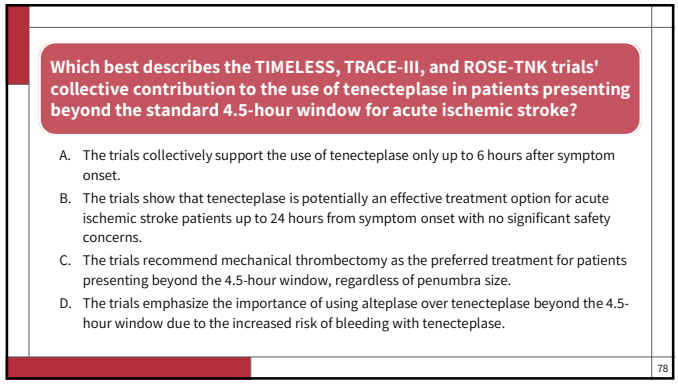

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Ms. Joan Vassos, a 62-year-old woman with a PMH of anxiety, presents 8 hours after the sudden onset of right-sided weakness, dysphasia, and slurred speech. CTA shows an occlusion in the right MCA, and perfusion imaging reveals a small ischemic core (25 mL) with a large penumbra (80 mL). Her NIHSS score is 15. This is her first ischemic stroke.

https://abc7news.com/post/joan-vassos-begins-journey-golden-bachelorette/15315472/ 79

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Based on the literature presented, could tenecteplase be an appropriate treatment option for this patient?

A. Yes; Her small infarct core and large penumbra make her a candidate for tenecteplase up to 24 hours after symptom onset.
B. Yes; She is having a mild stroke so tenecteplase is only indicated for mild strokes.
C. No; She is beyond the 4.5-hour window and should receive mechanical thrombectomy instead of thrombolysis.
D. No; Her occlusion is in the MCA so she should receive a mechanical thrombectomy instead.

https://abc7news.com/post/joan-vassos-begins-journey-golden-bachelorette/15315472/ 80

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References for Pharmacists

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THANK YOU!

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Critique

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Love at First Clot:

Can Tenecteplase Find Its Place Beyond the 4.5-Hour Window?

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