

# Tenecteplase (TNK) for Acute Ischemic Stroke- Starter Kit

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November 2021

# Tenecteplase for Ischemic Stroke: A "New" Thrombolytic

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Upstate University Hospital

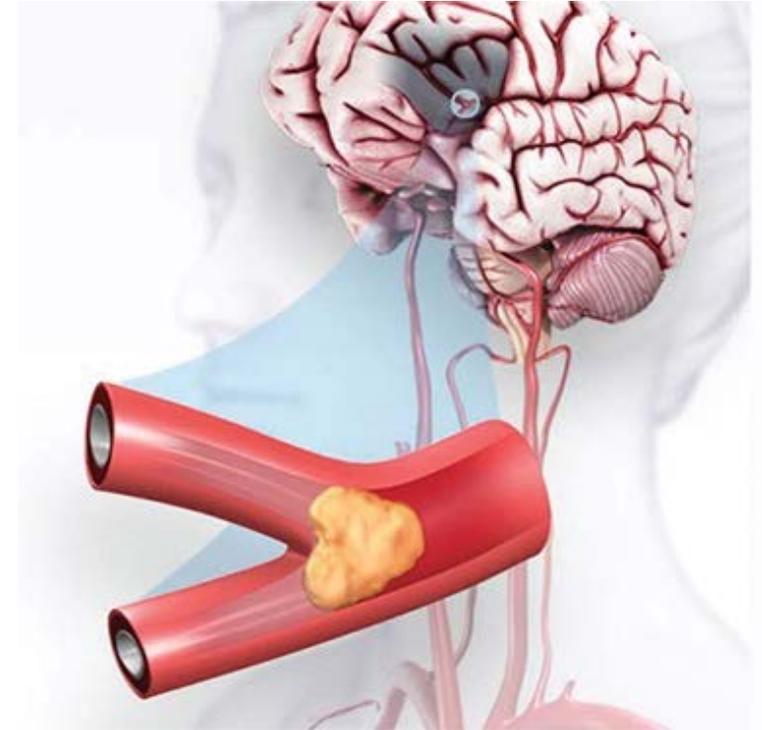
Syracuse, New York

# Disclosures

- Nothing to disclose

# Thrombolysis for Ischemic Stroke

- An ischemic stroke is an arterial blockage that decreases blood flow to the brain
- Decreased blood flow decreases oxygen and glucose delivery and causes cell death
- Restoring blood flow could prevent further cell death

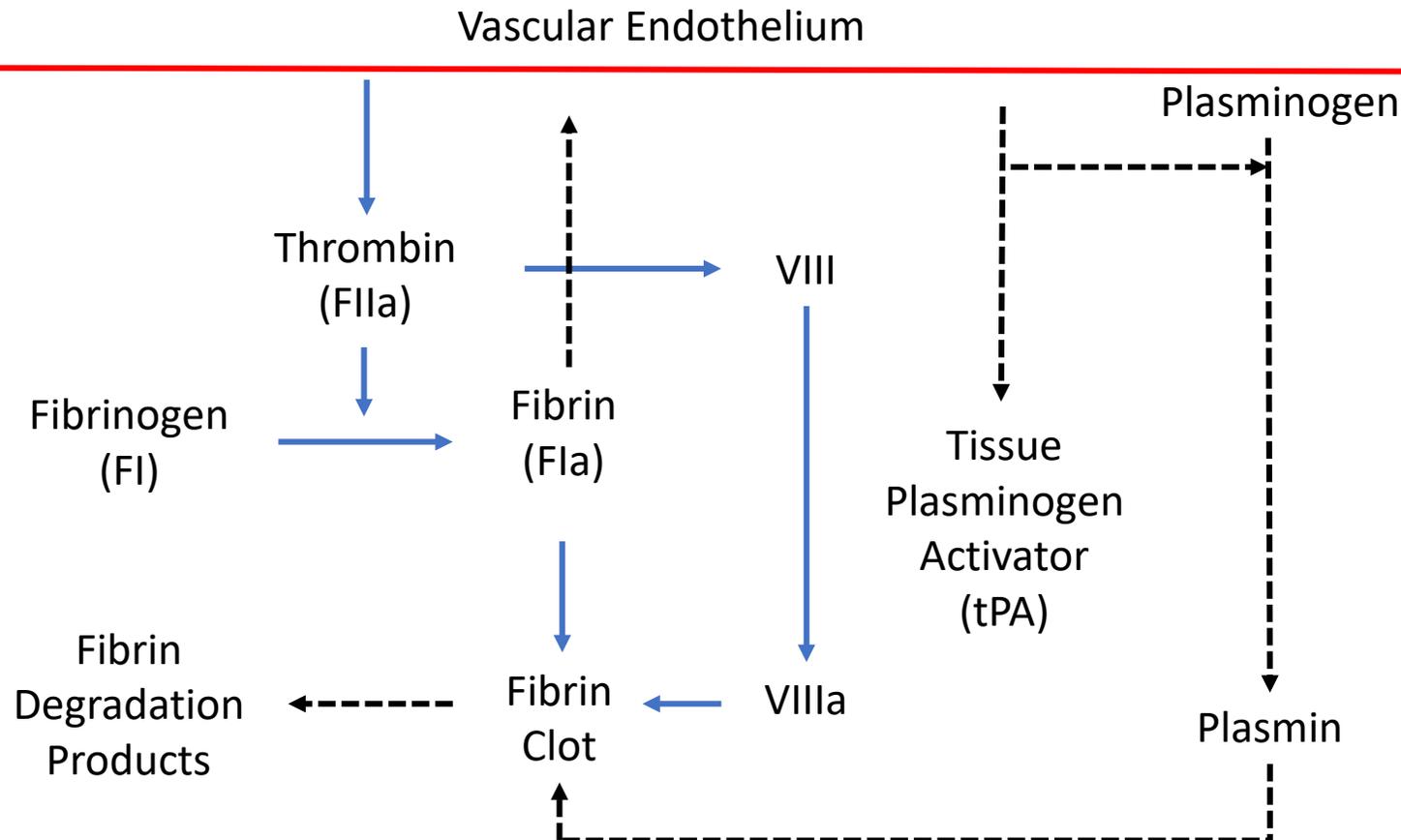


# Thrombolysis for Ischemic Stroke

## Fibrin Clot Formation & Breakdown: Basic Mechanism

### Tissue Plasminogen Activator (tPA)

- Natural fibrinolytic peptide
- Stimulated by fibrin formation
- Catalyzes plasminogen to plasmin conversion
- Plasmin degrades fibrin clots



**Increasing tPA could increase fibrin degradation & restore blood flow in ischemic stroke**

# Thrombolysis for Ischemic Stroke

What is the evidence supporting tPA administration in ischemic stroke???

## TISSUE PLASMINOGEN ACTIVATOR FOR ACUTE ISCHEMIC STROKE

THE NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE rt-PA STROKE STUDY GROUP\*

- Randomized, controlled trial (RCT) including 333 ischemic stroke patients with symptom onset within 3 hours
- IV recombinant tPA (r-tPA) vs. placebo
- **IV r-tPA associated with better functional outcomes at 3 months (number needed to treat = 8)**
- **IV r-tPA associated with more symptomatic intracranial hemorrhage (ICH) (number needed to harm = 17)**

*An additional study showed similar benefit and harm when extending the treatment window to 4.5 hours after the last known well*

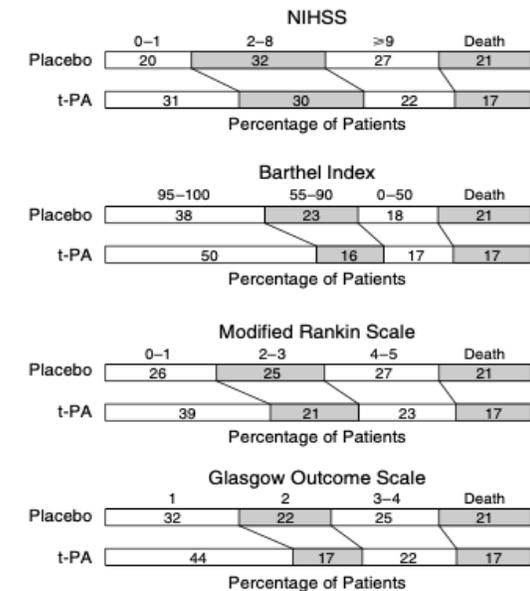


Figure 2. Outcome at Three Months in Part 2 of the Study, According to Treatment.

**Current guidelines recommend IV r-tPA in select ischemic stroke patients within 4.5 hours of symptom onset**

# Thrombolysis for Ischemic Stroke

What r-tPA do guidelines recommend in acute ischemic stroke???

## AHA/ASA GUIDELINE

**Guidelines for the Early Management of Patients With Acute Ischemic Stroke: 2019 Update to the 2018 Guidelines for the Early Management of Acute Ischemic Stroke: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association**

**Current guidelines recommend two r-tPAs**



## Alteplase (Activase®) [ALT]

Guideline preferred treatment

FDA approved for acute ischemic stroke within 4.5 hours of symptom onset



## Tenecteplase (TNKase®) [TNK]

Potential treatment in combination with mechanical thrombectomy

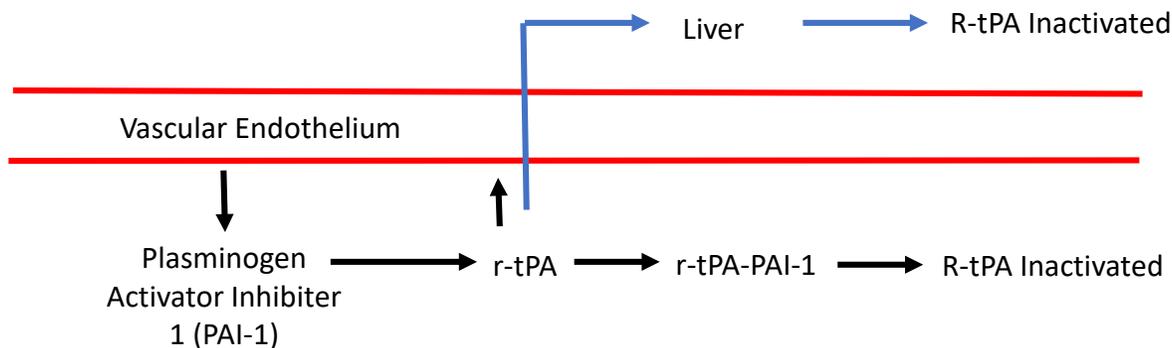
Alternative treatment in minor strokes without major intracranial occlusion

Not FDA approved for acute ischemic stroke (**Off-label indication**)

# ALT vs. TNK for Ischemic Stroke

## How are ALT & TNK Different???

### Drug Administration



- Both ALT & TNK are hepatically metabolized
- ALT is susceptible to inactivation by PAI-1
- TNK has greater PAI-1 resistance
- ALT has a shorter half-life (< 5 minutes) vs. TNK (> 20 minutes)
- ALT is eliminated from the body in ~ 20 minutes while TNK is eliminated in ~80 minutes

**ALT** → *Must be given as a bolus with infusion*

Recommended dose: 0.9 mg/kg up to 90 mg (10% bolus over one minute, 90% infusion over one hour)

**TNK** → *May be given as a bolus without infusion*

Studied doses: 0.1 - 0.4 mg/kg (100% as bolus over five seconds)

**TNK administration easier when compared to ALT**

# ALT vs. TNK for Ischemic Stroke

## How are ALT & TNK Different???

### Ease of Preparation & Administration

**ALT:** Bolus and infusion preparation

#### Materials required for ALT Preparation & Administration

1. ALT 100 mg kit containing lyophilized powder & diluent
2. Needles & syringes
3. Alcohol swabs
4. Saline flush for ALT bolus
5. Intravenous infusion pump for ALT infusion
6. Infusion pump tubing for ALT infusion
7. Saline flush bag for ALT infusion

**TNK:** Bolus preparation only

#### Materials required for TNK Preparation & Administration

1. TNK 50 mg kit containing lyophilized powder, diluent, needle, syringe and alcohol swabs
2. Saline flush for TNK bolus

**TNK requires fewer materials for preparation & administration**

# ALT vs. TNK for Ischemic Stroke

How are ALT & TNK Different???

## Medication Cost

	ALT (Activase®) 100 mg Vial	TNK (TNKase®) 50 mg vial
Pharmacy Acquisition Costs	\$ 8,179	\$5,780

\* Costs from our wholesale pharmacy distributor

**TNK costs approximately ~\$2,400 less per dose**

# ALT vs. TNK for Ischemic Stroke

## How are ALT & TNK Different???

### Summary

- 1. TNK administration is less complex vs. ALT** → TNK has a longer half-life allowing bolus administration alone. ALT has a shorter half-life & requires a bolus in combination with an infusion.
- 2. TNK preparation is less complex vs. ALT** → TNK requires fewer preparation materials.
- 3. TNK has a lower cost vs. ALT** → TNK pharmacy acquisition cost several thousand dollars less than ALT.

# ALT vs. TNK for Ischemic Stroke

**How do ALT & TNK Compare in Terms of Safety and Effectiveness???**

## **Ischemic Stroke (With or Without LVO and/or Mechanical Thrombectomy)**

**Burgos A, et al. Stroke 2019;  
50(8): 2156.**

**Huang X, et al. Int J Stroke  
2016; 11(5): 534.**

**Kheiri B, et al. J Thromb  
Thrombolysis 2018; 46(4): 440.**

- Three meta-analyses comparing ALT vs. TNK in acute ischemic stroke
- Each meta-analysis included 3 - 5 studies & between 250 – 1600 patients
- Some studies included LVO and some studies allowed mechanical thrombectomy
- Thrombolytic administration up to 3 - 6 hours after the last known well (most studies used up to 4.5 hours)
- ALT dosed per FDA labeling & TNK dosed as a 0.1 mg/kg, 0.25 mg/kg or 0.4 mg/kg bolus
- All three meta-analyses showed similar functional outcomes with ALT & TNK at three months
- All three meta-analyses showed similar ICH rates with ALT & TNK at three months

***TNK & ALT appear to have similar safety & effectiveness in ischemic stroke***

# ALT vs. TNK for Ischemic Stroke

## How do ALT & TNK Compare in Terms of Safety and Effectiveness???

### Ischemic Stroke with LVO

> [Stroke](#). 2020 Dec 4;STROKEAHA120030220. doi: 10.1161/STROKEAHA.120.030220.  
Online ahead of print.

#### Intravenous Thrombolysis With Tenecteplase in Patients With Large Vessel Occlusions: Systematic Review and Meta-Analysis

Aristeidis H Katsanos<sup>1</sup>, Apostolos Safouris<sup>2,3</sup>, Amrou Sarraj<sup>1,4</sup>, Georgios Magoufis<sup>3</sup>,  
Ronen R Leker<sup>5</sup>, Pooja Khatri<sup>6</sup>, Charlotte Cordonnier<sup>7</sup>, Didier Leys<sup>7</sup>, Ashkan Shoamanesh,  
Niaz Ahmed<sup>8,9</sup>, Andrei V Alexandrov<sup>10</sup>, Georgios Tsivgoulis<sup>2,10</sup>

*Only able to obtain abstract due to recent publication*

- Meta-analysis comparing TNK vs. ALT in ischemic stroke with LVO
- Four RCTs and > 400 patients
- TNK associated with increased odds for successful recanalization, functional improvement & mRS of 0 – 2 at three-months
- TNK & ALT associated with similar ICH rates, all cause-mortality, early neurologic improvement & mRS 0 – 1 at three-months

***TNK may provide more frequent reperfusion & functional benefit with similar safety when compared to ALT in ischemic stroke with LVO***

# ALT vs. TNK for Ischemic Stroke

**How do ALT & TNK Compare in Terms of Safety and Effectiveness???**

## Ischemic Stroke with LVO & Mechanical Thrombectomy



### Tenecteplase versus Alteplase before Thrombectomy for Ischemic Stroke

B.C.V. Campbell, P.J. Mitchell, L. Churilov, N. Yassi, T.J. Kleinig, R.J. Dowling, B. Yan, S.J. Bush, H.M. Dewey, V. Thijs, R. Scroop, M. Simpson, M. Brooks, H. Asadi, T.Y. Wu, D.G. Shah, T. Wijeratne, T. Ang, F. Miteff, C.R. Levi, E. Rodrigues, H. Zhao, P. Salvaris, C. Garcia-Esperon, P. Bailey, H. Rice, L. de Villiers, H. Brown, K. Redmond, D. Leggett, J.N. Fink, W. Collicutt, A.A. Wong, C. Muller, A. Coulthard, K. Mitchell, J. Clouston, K. Mahady, D. Field, H. Ma, T.G. Phan, W. Chong, R.V. Chandra, L.-A. Slater, M. Krause, T.J. Harrington, K.C. Faulder, B.S. Steinfurt, C.F. Bladin, G. Sharma, P.M. Desmond, M.W. Parsons, G.A. Donnan, and S.M. Davis, for the EXTEND-IA TNK Investigators\*

- RCT including ischemic stroke with LVO presenting within 4.5 hours of symptom onset
- TNK & ALT given prior to mechanical thrombectomy
- TNK 0.25 mg/kg IV up to 25 mg vs. ALT at FDA labeled dosing
- TNK had higher rate of reperfusion at initial angiographic assessment
- TNK had a lower median 90-day modified Rankin Score
- ALT & TNK had similar ICH rates

***TNK prior to thrombectomy associated with more frequent reperfusion & potentially better functional outcomes vs. ALT***

# ALT vs. TNK for Ischemic Stroke

## How do ALT & TNK Compare in Terms of Safety and Effectiveness???

### Cost Effectiveness

Stroke

#### CLINICAL AND POPULATION SCIENCES

### Cost-Effectiveness of Tenecteplase Before Thrombectomy for Ischemic Stroke

Lan Gao, PhD; Marj Moodie, DrPH; Peter J. Mitchell, MMed; Leonid Churikov, PhD; Timothy J. Kleinig, PhD; Nawaf Yassi, PhD; Bernard Yan, DMedSc; Mark W. Parsons, PhD; Geoffrey A. Donnan, MD; Stephen M. Davis, MD; Bruce C.V. Campbell, PhD; for the EXTEND-IA TNK Investigators

- Post-hoc economic analysis from the RCT comparing TNK vs. ALT in ischemic stroke with LVO & mechanical thrombectomy
- TNK not associated with lower total 90-day cost
- TNK associated with lower lifetime total costs
- TNK more effective in short and long-term
- TNK had a 97.4% - 100% probability of being cost-effective vs. ALT in ischemic stroke with LVO & mechanical thrombectomy

***TNK maybe more cost-effective vs. ALT in some ischemic stroke patients***

# ALT vs. TNK for Ischemic Stroke

**How do ALT & TNK Compare in Terms of Safety and Effectiveness???**

## **Summary**

1. TNK appears to be at least as safe & effective vs. ALT in ischemic stroke
2. TNK may have potential additional benefit in some ischemic stroke populations, most notably LVO undergoing mechanical thrombectomy
3. TNK may be more cost-effective vs. ALT in some ischemic stroke populations

***Are experts considering using TNK over ALT in ischemic stroke???***

# ALT vs. TNK for Ischemic Stroke

**Some Experts are Now Recommending Clinicians Consider TNK over ALT in Ischemic Stroke**

[West J Emerg Med](#). 2020 Mar; 21(2): 199–202.

PMCID: PMC7081848

Published online 2020 Feb 24. doi: [10.5811/westjem.2020.1.45279](https://doi.org/10.5811/westjem.2020.1.45279)

PMID: [32191176](https://pubmed.ncbi.nlm.nih.gov/32191176/)

## Using Tenecteplase for Acute Ischemic Stroke: What Is the Hold Up?

[Tony Zitek](#), MD,<sup>✉†</sup> [Ramsey Ataya](#), MD,<sup>\*</sup> and [Isabel Brea](#), MD<sup>†</sup>

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### Conclusion

Tenecteplase is at least as effective as alteplase with regards to neurologic improvement after treatment of acute ischemic stroke. Additionally, tenecteplase is less expensive, easier to administer, and may have less bleeding complications than alteplase. Thus, physicians should consider using tenecteplase rather than alteplase for thrombolysis of acute ischemic stroke. If used, the preferred dose of tenecteplase is 0.25 mg/kg (maximum 25 mg).

# ALT vs. TNK for Ischemic Stroke

## Some Experts are Now Recommending Clinicians Consider TNK over ALT in Ischemic Stroke

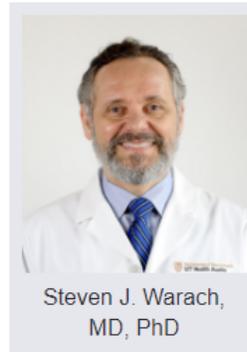
- Medical center adopted TNK over ALT in ischemic stroke
- Institution recognizes transition is neither FDA or guideline approved
- TNK safety & effectiveness appear similar vs. ALT
- TNK administered more quickly, had fewer administration errors and was less costly

### ISC 2020: Switching to Tenecteplase as Lytic of Choice for Acute Ischemic Stroke Feasible, May Save Time

An ongoing study suggests a key benefit may be shorter delays to thrombectomy for transfer patients

PracticeUpdate Editorial Team

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Steven J. Warach,  
MD, PhD

February 20, 2020—Los Angeles, CA—A switchover from alteplase to tenecteplase as the standard of care thrombolytic for acute ischemic stroke reduced door-to-needle times and resulted in similar outcomes, no safety concerns, and cost savings in an American multihospital network. The findings were presented here at the 2020 International Stroke Conference, taking place from February 19 to 21.

“The impetus for the study was the mounting evidence that switching from alteplase to tenecteplase could have some practical, if not clinical, benefits first in the context of [ST segment elevation myocardial infarction \(STEMI\)](#), then [ischemic stroke](#),” presenter Steven J. Warach, MD, PhD, of the University of Texas Southwestern Medical Center in Austin, told Elsevier’s *PracticeUpdate*. He noted that the biggest advantage of tenecteplase in the stroke setting is that it can be

# ALT vs. TNK for Ischemic Stroke

**Some Experts are Now Recommending Clinicians Consider TNK over ALT in Ischemic Stroke**

## Viewpoint

July 20, 2020

### **Stroke Thrombolysis With Tenecteplase to Reduce Emergency Department Spread of Coronavirus Disease 2019 and Shortages of Alteplase**

Steven J. Warach, MD, PhD<sup>1,2</sup>; Jeffrey L. Saver, MD<sup>3</sup>

[» Author Affiliations](#) | [Article Information](#)

*JAMA Neurol.* 2020;77(10):1203-1204. doi:10.1001/jamaneurol.2020.2396

**Why Aren't More Institutions using TNK over ALT for Ischemic Stroke???**

- Editorial written about TNK benefits in the time of COVID-19
- Written by the physician from the previous slide
- TNK could decrease staff-patient exposure vs. ALT given its bolus only administration
- TNK obviates infusion pump need and could decrease viral transmission via ward-to-ward medical device transfer

# ALT vs. TNK for Ischemic Stroke

## Why Aren't More Institutions Using TNK over ALT for Ischemic Stroke???

### TNK is not FDA Approved for Ischemic Stroke

- Unclear if FDA is considering approving TNK for ischemic stroke
- There are at least five TNK studies recruiting stroke patients on [clinicaltrials.gov](https://clinicaltrials.gov)

**Institutions should likely assess these considerations before system wide TNK adoption in ischemic stroke**

### TNK is not the Guideline Preferred Thrombolytic for Ischemic Stroke

- ALT → guideline preferred thrombolytic
- ALT → More experience & familiarity
- Confusing TNK recommendations in 2019 guideline update
  - Maybe reasonable to use TNK over ALT in ischemic stroke eligible for thrombectomy
  - TNK maybe considered in minor stroke without major intracranial occlusion

### Optimal TNK Dosing in Ischemic Stroke is Unclear

- Studies utilized TNK doses of 0.1 mg/kg, 0.25 mg/kg and 0.4 mg/kg in ischemic stroke
- All doses at least as effective vs. ALT
- All doses had similar safety vs. ALT
- TNK 0.25 mg/kg with thrombectomy may be more effective vs. ALT with thrombectomy
- There maybe a trend towards increased bleeding with TNK 0.4 mg/kg vs. other TNK doses

### TNK Treatment Window Unclear

- Unclear if treatment window same or different vs. ALT
- Most clinical trials have used a treatment window of 3 – 6 hours after the last know well
- TNK at least as safe and effective vs. ALT at all time points
- Most TNK studies used a 4.5-hour window from the last know well so this is likely most appropriate

# Tenecteplase for Ischemic Stroke

## Summary

- TNK is an ALT alternative not currently FDA approved for ischemic stroke
- TNK is easier to prepare, easier to administer & less costly vs. ALT
- TNK appears to be at least as safe & effective vs. ALT in ischemic stroke & maybe more effective with LVO undergoing mechanical thrombectomy
- The role of TNK in the ischemic stroke guidelines is a little unclear but it appears it can at least be considered over ALT in patients eligible for mechanical thrombectomy
- There are some unanswered questions on how to use TNK in ischemic stroke, but the evidence is strongly encouraging

## Indications for thrombolytic use

**Indication for use: Both IV Alteplase (ALT) and IV Tenecteplase (TNK) have been proven effective in the treatment of acute ischemic stroke (AIS). IV Alteplase can also be used in the treatment of central retinal artery occlusion (CRAO).**

- 1. IV Alteplase can be utilized for the treatment of AIS or CRAO within 0-3 hours of the last know well (LKW), or 3-4.5 hours of LKW with additional considerations. The use of Alteplase in the 4.5-9-hour window is also acceptable in conjunction with specific imaging, considerations, and written consent from the patient/family/proxy decision-maker.**
- 2. IV Tenecteplase can be utilized for the treatment of AIS within 0-4.5 hours of last known well**

# Thrombolytic Consent

Informed consent is to be obtained if the patient remains a candidate for thrombolytics.

1. (Alteplase and Tenecteplase) For symptom onset < 4.5 hours, verbal informed consent will be performed with the patient/family/proxy treatment team and documentation will be in the medical record.
2. (For Alteplase only) For symptom onset > 4.5 hours, written consent for administration will be obtained from the patient/family/proxy and documented

# TNK Order Panel in EMR

## Tenecteplase Panel

✓ Accept

sodium chloride (preservative free) 0.9 % flush 10 mL

Remove

10 mL, Intravenous, Once, today at 0715, For 1 dose  
Please flush line BEFORE administration of tenecteplase.

And

tenecteplase (TNKASE) injection 13.6 mg

Remove

13.6 mg (0.25 mg/kg × 54.4 kg), Intravenous, Once, today at 0715, For 1 dose  
Flush tenecteplase with 10 mL of Sodium Chloride 0.9% immediately after administration.

And

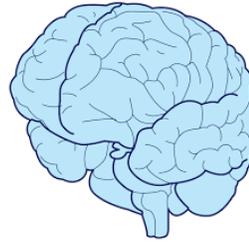
sodium chloride (preservative free) 0.9 % flush 10 mL

Remove

10 mL, Intravenous, Once, today at 0715, For 1 dose  
Please flush line AFTER administration of tenecteplase.

# Tenecteplase Dosing

- The total dose of Tenecteplase will be given IV push only (pushed over five seconds)
- Tenecteplase is dosed at 0.25 mg/kg with a maximum dose of 25mg, with a 10ml 0.9% NaCl flush before and after bolus to clear the IV line.
- Tenecteplase is reconstituted with provided diluent.
- The RN will STAT page treatment team and prepare for a repeat CT scan should there be a decline in neuro status.



Staff Education

### Tenecteplase (TNKase®) [TNK]

- **Alternative** treatment in minor strokes without major intracranial occlusion
- Not FDA approved for acute ischemic stroke (**Off-label indication**)
- Recommended in 2018 American Heart Guidelines as possible superior alternate to Alteplase

	Tenecteplase	Alteplase
<b>Dosing</b>	<b>0.25mg/kg MAX DOSE 25mg</b>	0.9 mg/kg MAX DOSE 90mg 10% bolus over one minute, 90% infusion over one hour
<b>Dosing Style</b>	<b>Bolus Dose only (pre and post IV line flush)</b>	Bolus, infusion and 50 ml flush (~1.5 hours)
<b>Cost</b>	<b>\$5,780 per 50mg vial</b>	\$8,179 per 100mg vial
<b>Metabolization</b>	<b>Liver</b>	Liver
<b>Half-life</b>	<b>&gt;20 minutes</b>	< 5 minutes
<b>Effectiveness</b>	<b>Tenecteplase prior to thrombectomy was associated more frequent reperfusion &amp; better functional outcomes (lower 90-day mRS)</b>	
<b>Hemorrhagic conversion</b>	<b>Similar hemorrhage rate to Alteplase</b>	

# Nursing Monitoring

## Monitoring

- Neuro VS *within* 15 minutes of bolus
- Neuro VS every 15 minutes x 2 hours
- Neuro VS every 30 minutes X 6 hours
- Neuro VS every 1 hour X 16 hours

\*Total of 24 hours intensive monitoring\*

Monitor for signs of orolingual angioedema (tongue swelling, difficulty breathing)

Monitor for signs of hemorrhagic conversion (changing mental status) → page stroke team

## Blood Pressure

Pre-thrombolytic BP: **SBP < 185 AND DBP < 110**

During infusion + 24 hours after: **SBP < 180 DBP < 105**

## Additional References

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