KANSAS INITIATIVE FOR STROKE SURVIVAL

A PROJECT BY AND FOR KANSANS

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IV Tenecteplase Thrombolysis in Acute Stroke

"First Tuesdays" Lecture Series

Introduction and Goal of “First Tuesdays”

- Sabreena Slavin MD – Vascular Neurologist and Neurohospitalist at KU School of Medicine
- Didactic lecture series as part of the Kansas Initiative for Stroke Survival
- Updates in Practice and FAQ’s on Acute Stroke Care
- 30 minutes of didactic/question and answers

Previous recommendations on IV alteplase

- Indicated for all patients with acute ischemic stroke with disabling symptoms
- Many contraindications: including cerebral hemorrhage, history of recent major stroke or bleed, recent invasive surgeries, any anticoagulation use (except warfarin if INR is subtherapeutic), thrombocytopenia/coagulopathies
- Dose: 0.9 mg/kg up to 90 mg max; 10% given as bolus over 1 minute and 90% given as a drip over 1 hour
- Time window: Last well up to 4.5 hours and more recently up to 9 hours or with wakeup symptoms if meets certain imaging parameters

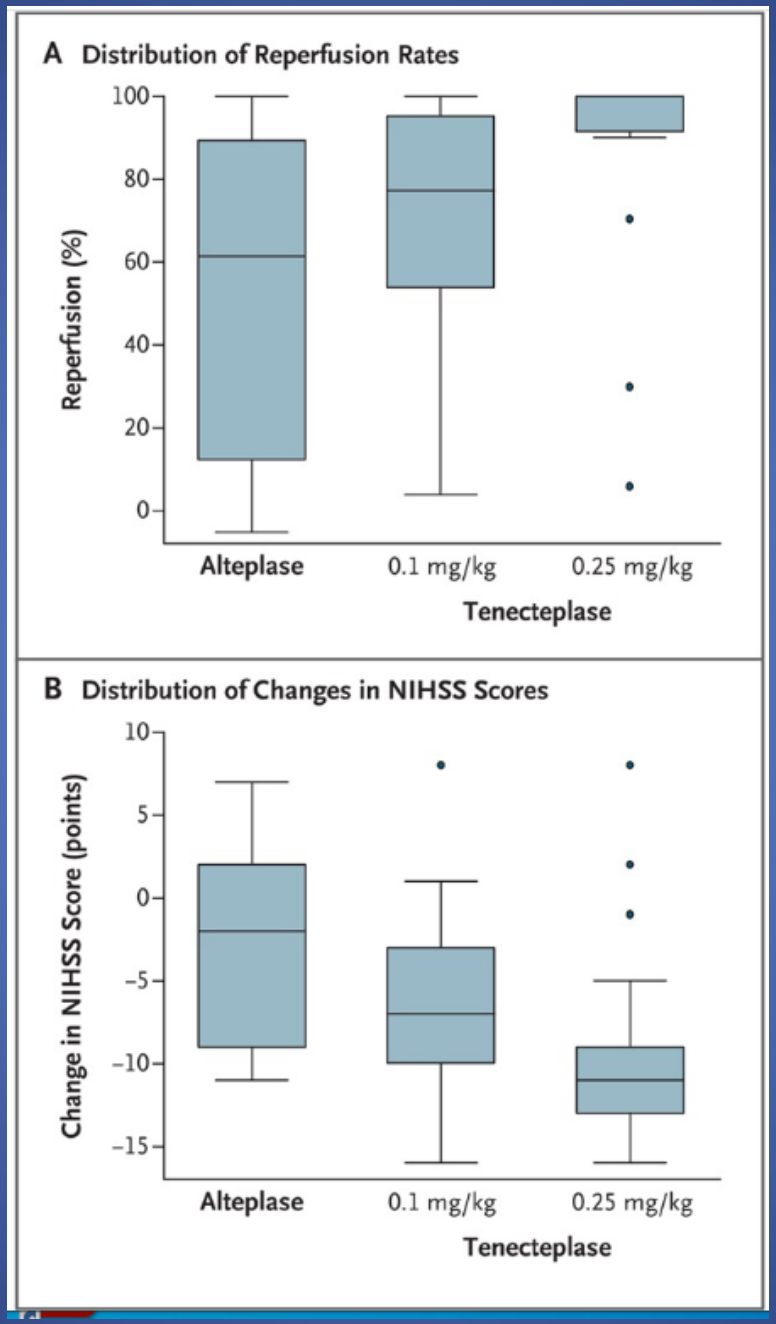
Tenecteplase (TNK)

- Has better fibrin specificity
- Longer half life (>20 minutes)
- Approved for acute MI
- Given as single dose vs bolus/drip which can make admin easier. Given over 5-10 seconds
- Easier preparation may reduce times to treatment
- Less expensive
- Still off-label use: must still have alteplase on formulary and patient/family must agree to use
- Contraindications and reversals same at alteplase

Early RCT on TNK

- Phase 2B RCT in patients with ischemic stroke who had perfusion deficit on CTP greater than 20% of core deficit: randomizing to alteplase vs two different doses of TNK (0.1 mg/kg or 0.25 mg/kg)
- 75 total patients. Both TNK groups had greater reperfusion and clinical improvement at 24 hours than alteplase group, and 0.25 mg/kg dose was superior. No differences in bleeding or adverse events.

Parsons et al, *NEJM* 2012



Parsons et al, *NEJM* 2012

ATTEST trial

- Phase 2 RCT in patients with ischemic stroke in Scotland: randomized to SOC alteplase or TNK 0.25 mg/kg; no imaging parameters beyond CT brain w/o contrast.
- 104 patients enrolled: No difference in symptomatic ICH or total ICH between groups, but trend towards total ICH favoring TNK (15% vs 29%)

Huang et al, *Lancet Neurol* 2015

TNK + Thrombectomy?

- RCT in patients with acute ischemic stroke of ICA, MCA, or basilar: randomized to alteplase vs TNK 0.25 mg/kg. Primary outcome was reperfusion of greater than 50% of involved territory at angiogram.
- 202 patients enrolled: Primary outcome occurred in 22% of patients with TNK vs 10% with alteplase (incidence ratio 2.2, 95% CI 1.1-4.4). TNK also had better 90 day functional outcome. No difference in symptomatic ICH.

Campbell et al, *NEJM* 2018

TNK + Thrombectomy (higher dose)?

- Multicenter RCT of acute ischemic stroke in patients with LVO: randomized to open label 0.4 mg/kg vs 0.25 mg/kg TNK prior to EVT. Main outcome was reperfusion of greater than 50% involved territory during angiogram.
- 300 patients enrolled: Reperfusion occurred in 19.3% of BOTH groups. No differences in any functional outcomes, deaths, or symptomatic ICH

Campbell et al, *JAMA* 2020

NOR-TEST

- Phase 3 open label RCT in patients with acute ischemic stroke: randomized to alteplase vs TNK 0.4 mg/kg. Primary outcome was mRS of 0-1 at 3 months.
- 1100 patients enrolled. ***Had high prevalence of minor stroke.*** Primary outcome was achieved by 64% of patients in TNK group and 63% of patients in alteplase group (no difference). Death rates and serious adverse events were the same.

Logallo et al, *Lancel Neurol* 2017

Stroke Guidelines 2019 Update

- “It may be reasonable to choose Tenecteplase (single IV bolus of 0.25 mg/kg over IV alteplase in patients without contraindications for IV fibrinolysis who are also eligible to undergo mechanical thrombectomy.”
- “Tenecteplase administration as a 0.4 mg/kg single IV bolus has not been proven to be superior or noninferior to alteplase but might be considered as an alternative to alteplase in patients with minor neurological impairment and no major intracranial occlusion.”

Powers et al, *Stroke* 2019

Higher dose of TNK safety concern

- Phase 3 RCT in patients with moderate-severe ischemic stroke (NIHSS ≥ 6): randomized to alteplase vs 0.4 mg/kg TNK. Primary outcome was mRS 0-1 at 3 months.
- 216 patients enrolled, but trial stopped early. Favorable outcome was achieved in 32% of patients with TNK vs 51% of patients with alteplase. Any ICH was also more frequent (21% TNK vs 7% alteplase) and mortality was higher (26% TNK vs 5% alteplase).

Kvistad et al, *Lancel Neurol* 2022

Review of available data from trials

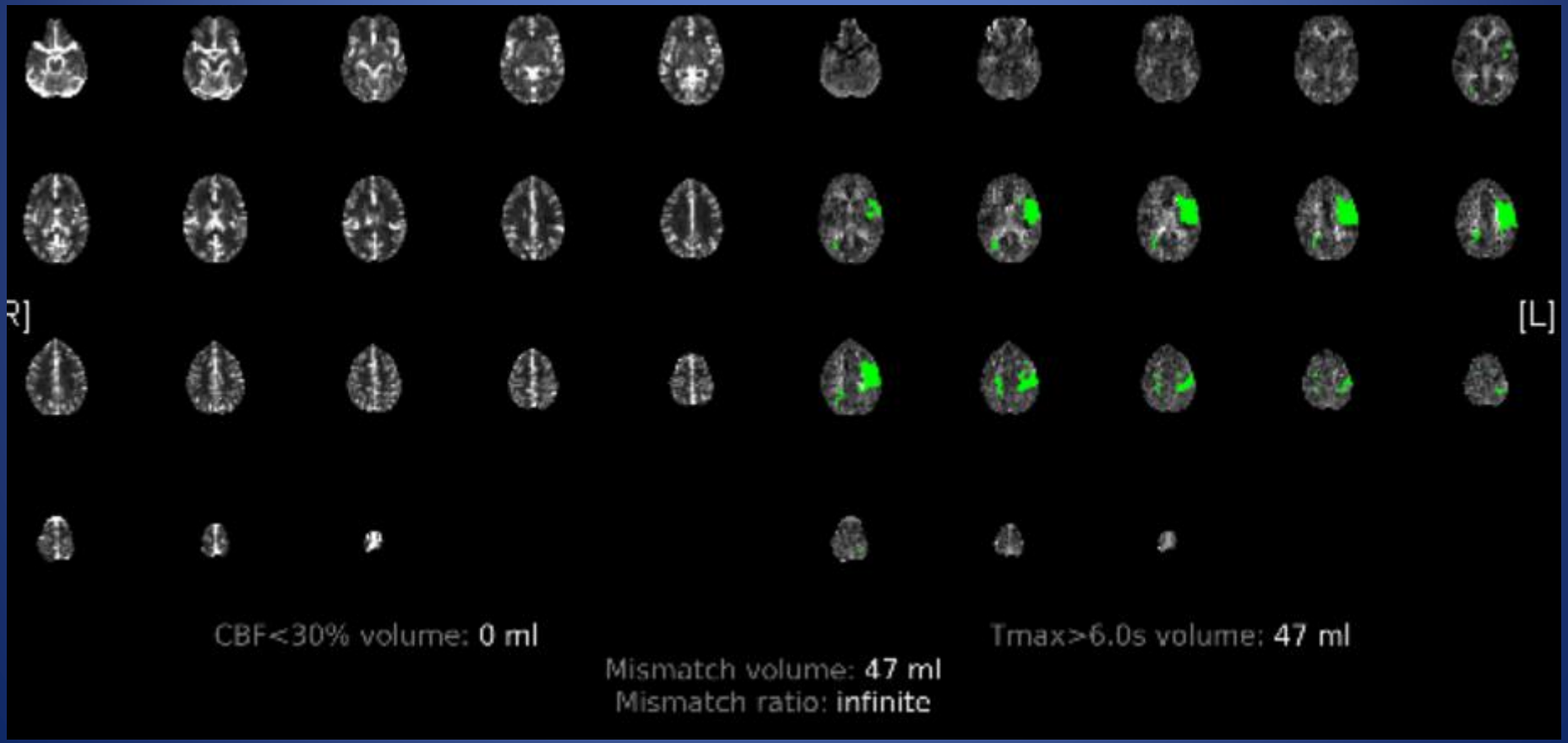
- TNK dose 0.25 mg/kg over 0.1 mg/kg or alteplase leads to superior clinical improvement
- TNK dose 0.25 mg/kg over alteplase has trend towards fewer sICH
- TNK dose 0.25 mg/kg is better than alteplase at reperfusion before thrombectomy in LVO cases and equivalent to 0.4 mg/kg
- TNK dose 0.4 mg/kg has equivalent outcomes to 0.25 mg/kg in minor stroke and may be worse than alteplase in moderate to severe strokes

TNK past 4.5 hours?

- TIMELESS: Compare efficacy of **Tenecteplase 0.25 mg/kg** (maximum 25 mg) vs placebo in acute ischemic stroke patients in 4.5 - 24 hours from last well
- Needs to have an ICA, M1, or M2 occlusion and NIHSS ≥ 5
- Needs to have CTP with core volume < 70 mL, mismatch volume ≥ 15 mL, and mismatch ratio ≥ 1.8
- Primary outcome will be 90 day mRS ordinal analysis
- Plan to enroll 456 patients total

Imaging Criteria

- CTP with core volume < 70 mL, mismatch volume ≥ 15 mL, and mismatch ratio ≥ 1.8



Data from KUMC

- 10 patients received TNK so far
- No complications in any
- 9 with final diagnosis of ischemia, 1 more likely mimic
- 9 patients discharged home (1 patient discharged to inpatient rehab)
- Discharge mRS: 0-1 in 8 patients, 2 in 1 patient

Questions?

- Call for help anytime!
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