Making the Change: TNK for Acute Ischemic Stroke

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TNK vs ALT

Tenecteplase, which was initially approved in June of 2000 for reduction of mortality associated acute myocardial infarction (MI), is a modified form of human tissue plasminogen activator (tPA) with multiple point mutations of alteplase. It promotes initiation of fibrinolysis by binding to fibrin and converting plasminogen to plasmin. When compared to alteplase, it is more fibrin specific and more resistant to plasminogen activator inhibitor-1 (PAI-1), with a longer duration of action. This allows TNK to be administered as a single bolus over 5 seconds, without the need for infusion and post infusion flush. This give-and-go thrombolytic allows your facility to quickly administer medication and move your patient to the ICU, IR, or a higher level of care.

Dosing

There have randomized control trials looking at TNK vs ALT for acute ischemic stroke treatment. These three trials have used different dosages of TNK; 0.1 mg/kg, 0.25 mg/kg, and 0.4 mg.kg. From literature review OHSU settled on 0.25 mg/kg as our dosing of choice. This dose used in EXTEND-IA TNK was found to have higher recanalization rates vs ALT (22% TNK vs. 10% ALT).

Administration

One of the biggest advantages of TNK over ALT is the ease of administration. ALT requires whom ever is mixing the drug to draw up the correct bolus, draw up the correct infusion, and waste the remainder when necessary. Your nurses also need to set up a pump, prime the line, and ensure that the 50ml flush is available. ALT bolus is given over two minutes and then the infusion runs for 1 hour, and finally a 50ml flush is administered. Don't forget to document all of your stop and start times as well.
TNK requires that whom ever is mixing the medication to draw up the appropriate bolus and waste the remainder. The drug is then pushed over 5 seconds and flushed with saline. At this point you are done.

Assessment & Documentation

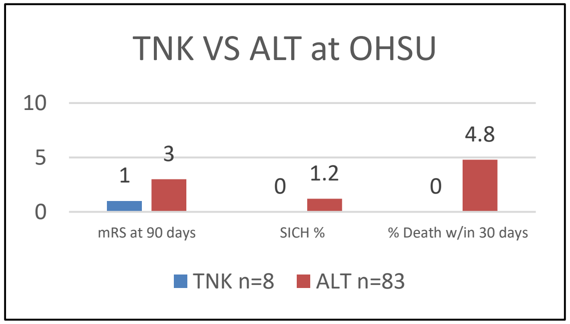
One of the key advantages to making the change to TNK is that you will not need to make any changes to your documentation of assessments standards.

Implementation & Training

Though not as seamless of a change as with the assessment and documentation, implementation and training for TNK is not a resource heavy endeavor. At OHSU we focused training on ED RN's and ED pharmacists. Nurses were provided in-time education at huddles and staff meetings. Also, we have updated our new hire/annual education to include TNK administration.
Pharmacists educated their team at their monthly staff meeting. This was more of an FYI as this team was already familiar with TNK since we use it in the cardiac setting.

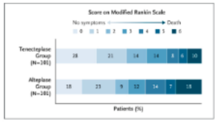
Our Experience

To date we have treated 9 patients with TNK. We have experienced no complications and all but 2 of these patients had a mRS of 0-1 at 90 days. Our staff also express increased satisfaction with the change. They mention the ease of administration and not needing to set up the pump or flush as the main drivers of increased satisfaction.

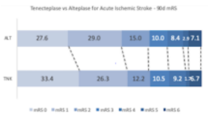


Recent Trails & Enrolling Clinical Trials

Nor-Test:
A randomized control trail (RCT) comparing 0.4 mg/kg TNK vs 0.9 mg/kg ALT with an endpoint looking for noninferiority. NORTEST enrolled 1100 patients and they found that TNK was neither inferior nor superior to ALT in patients who had small vessel strokes.
EXTEND-IA TNK:
A RCT comparing 0.25 mg/kg TNK to 0.9 mg/kg ALT for patients who have a LVO. 202 patients were enrolled in this trail. TNK or ALT was administered, 30 min later the patient was taken to IR for angiography and thrombectomy if needed. EXTEND-IA TNK found that 22% of the TNK patients had successful recanalization while on 10% of ALT patients had successful recanalization.



Meta Analysis:
In August 2019 Burgos and Saver published a Meta-analysis of all RCT to date that compared TNK to ALT. They included 5 RCT's that enrolled 1585 patients in their analysis. These RCT's used varying doses of TNK from 0.1mg/kg, 0.25mg/kg, and 0.4mg/kg. Even with the different dosages they determined that TNK is not inferior to ALT. Their recommendation is to perform a dosing trial to determine which dose of TNK is most appropriate.



TIMELESS:
A randomized control trail exploring TNK vs standard of care for patients 4.5 to 24 hours from last know well. Through the use of perfusion imaging patients are identified. Patients can be enrolled if they have a core less than 70ml and a mismatch of at least 1.8. This trial is currently enrolling.

References available upon request