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Intravenous tenecteplase compared with alteplase for acute ischemic stroke in Canada (AcT): a pragmatic, multicentre, open-label, registry-linked, randomised, controlled, non-inferiority trial

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Article Type: Therapy

Ratings: *Methods*—4.5/5, *Usefulness*—5/5

Introduction

Background

Alteplase (tPA) given as a bolus followed by an infusion is the current recommended thrombolytic therapy for acute ischemic stroke (AIS) for those eligible for treatment.

Objectives

Menon and colleagues sought to compare single bolus tenecteplase (TNK) to tPA for reperfusion of patients with AIS.

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Methods

Design

The AcT trial was a multicentre, open-label, registry-linked, randomized, controlled, non-inferiority trial.

Setting

22 primary and comprehensive stroke centres across Canada.

Subjects

Patients (age ≥ 18 years) presenting with AIS within 4.5 h and eligible for thrombolytic therapy.

Intervention

The AcT trial compared TNK 0.25 mg/kg bolus (maximum 25 mg) with tPA 0.9 mg/kg (0.09 mg/kg bolus followed by 0.81 mg/kg infusion; maximum 90 mg) as treatment for AIS.

Outcomes

Primary outcome was the proportion of patients with modified Rankin Scale (mRS) 0–1 at 90–120 days after randomization. Safety outcomes included symptomatic intracranial hemorrhage within 24 h, orolingual angioedema within 24 h, extracranial bleeding requiring transfusion within 24 h and 90-day all-cause mortality.

Results

Of the 1600 patients included in the study, 1577 were included in the intention to treat population ($n=806$ in TNK and $n=771$ in tPA). Door to needle times were 36 min in the TNK group and 37 min in tPA group. The mean onset of symptoms to thrombolysis were similar in both groups (128 min TNK and 131 min tPA). The mean NIHSS score was 9 in the TNK group and 10 in the tPA group.

296 (36.9%) of 802 patients who received TNK had an excellent neurologic outcome with a mRS of 0–1 at 90–120 days compared to 266 (34.8%) of 765 patients who received. This met their pre-specified non-inferiority threshold with an unadjusted risk difference of 2.1%.

Appraisal

Strengths

- Pragmatic RCT with large sample size
- Outcome measures were objective and patient-centred
- Eligibility criteria aligns with international guidelines for treatment of AIS
- Low loss to follow-up at 90 days (0.6%)

Limitations

- Open-label design
- Does not identify patients baseline mRS

Context

The main thrombolytic agent for AIS since the 1990s has been tPA delivered as a bolus followed by infusion. TNK has potential advantages including increased fibrin specificity, a longer half-life, and is administered as a bolus without the need for infusion, which may reduce medical errors [1].

Prior studies have demonstrated that 0.4 mg/kg TNK was not superior 0.9 mg/kg tPA [2] and that 0.4 mg/kg TNK has greater rates of symptomatic ICH and worse clinical outcomes than 0.25 mg/kg TNK [3]. There was no prior comparison of TNK at the 0.25 mg/kg dose compared to 0.9 mg/kg tPA.

Local stroke neurologists support the use of single-bolus TNK for the treatment of AIS in eligible patients. Canadian stroke centers including Ottawa and Calgary are in the process of making this practice change.

Bottom line

The use of TNK 0.25 mg/kg as a single bolus for the treatment of AIS is similar to tPA with respect to neurologic function and safety. This is a practice changing paper. The results of this trial and the practical advantages of a single-bolus regimen with TNK will likely change standard of care for thrombolysis of acute ischemic stroke.

Data availability Data is available upon request to the authors.

Declarations

Conflict of interest The authors have no conflicts of interest to declare.

References

1. Tanswell P, Modi N, Combs D, Danays T. Pharmacokinetics and pharmacodynamics of tenecteplase in fibrinolytic therapy of acute myocardial infarction. Clin Pharmacokinet. 2002;41:1229–45.
2. Logallo N, et al. Tenecteplase versus alteplase for management of acute ischaemic stroke (NOR-TEST): a phase 3, randomised, open-label, blinded endpoint trial. Lancet Neurol. 2017;16:781–8.
3. Kvistad CE, et al. Tenecteplase versus alteplase for the management of acute ischaemic stroke in Norway (NOR-TEST 2, part A): a phase 3, randomised, open-label, blinded endpoint, non-inferiority trial. Lancet Neurol. 2022;21:511–9.