Online Supplement Methods

Trials description

The Australia-TNK and ATTEST trials were Prospective, Randomised, Open, Blinded End-point (PROBE) studies comparing the efficacy and safety of alteplase and tenecteplase in thrombolysis-eligible patients with acute ischaemic stroke, using clinical and imaging biomarkers for outcome evaluation. The Australia-TNK study recruited from three sites and ATTEST was a single centre study. For both studies, patients were eligible if they had a clinically diagnosed supratentorial acute ischaemic stroke with a measurable deficit on the NIH stroke scale (NIHSS), were aged ≥18 years, were living independently pre-stroke, and were considered eligible for intravenous thrombolysis according to local clinical guidelines. Both studies included patients over 80 years of age. Both trials excluded patients with major early ischemic change on non-contrast CT (NCCT). In ATTEST, patients had to be presenting to hospital within 4.5 hours of symptom onset, and in the Australian study patients were included up to 6 hours post-onset. In ATTEST, patients were randomised to either tenecteplase 0.25mg/kg or alteplase 0.9mg/kg treatment on a 1:1 basis. The Australia-TNK trial randomised patients to alteplase 0.9mg/kg or one of two doses of tenecteplase (0.1 mg/kg or 0.25 mg/kg) on a 1:1:1 basis. This analysis pooled trial data on patients receiving the 0.25 mg/kg tenecteplase dose or 0.9 mg/kg alteplase, and excluded the 0.1mg/kg group. A key inclusion criteria difference between the two trials was that for Australia-TNK, patients were required to have a 'dual-target': visible CTP mismatch (by qualitative assessment), and an intracranial vessel occlusion on CTA (excluding internal carotid artery occlusions). ATTEST used standard of care NCCT thrombolysis eligibility, but obtained multimodal CT imaging (CTP and CTA) following randomisation. Initial stroke severity evaluated by NIHSS score was measured in all patients acutely and at 24 hours, while resulting disability was

assessed using the modified Rankin Scale (mRS, range 0-6 0 being no disability and 6 being death) at 90 days in a blinded fashion.