Letter by Behrouz et al Regarding Article, “Tenecteplase–Tissue-Type Plasminogen Activator Evaluation for Minor Ischemic Stroke With Proven Occlusion”

To the Editor:

The study by Coutts et al on intravenous tenecteplase for minor strokes is a reminder, once again, that a large-scale trial involving this drug in acute ischemic stroke is needed. Although the study was small and uncontrolled, it reiterated what earlier investigations have suggested about the safety and efficacy of tenecteplase. In tenecteplase–tissue-type plasminogen activator evaluation for minor ischemic stroke with proven occlusion-1, no comparison to historical alteplase cases could be made because, as the authors acknowledged, patients with minor strokes are excluded or under-represented in most of the stroke thrombolysis trials. The investigators could, nonetheless, compare their results to a matched control group of patients who did not receive any thrombolytics, which is typically the case with minor strokes.

There are indications that tenecteplase may be a superior thrombolytic to alteplase. Existing data suggest higher recanalization rates and better 90-day clinical outcomes with tenecteplase. However, the reluctance to test tenecteplase in the United States owes to the uncertain results of previous tenecteplase/alteplase trials. A phase Ib/III randomized trial of tenecteplase versus alteplase in the 0- to 3-hour acute ischemic stroke window was prematurely terminated because of slow enrollment. The study compared 3 different doses of tenecteplase (0.1, 0.25, and 0.4 mg/kg) to alteplase. The 0.4 mg/kg dose was eliminated as inferior, yet this same dose is being applied in an ongoing Norwegian trial.

To survey existing study results, we combined the total number of patients who received tenecteplase at doses ≤0.4 mg/kg in the pilot with the phase Ib/III US studies and compared them with the alteplase and placebo arms of the National Institutes of Neurological Disorders and Stroke–Tissue-Type Plasminogen Activator (NINDS-TPA) trial. In the 2 studies, 156 patients received tenecteplase at doses ≤0.4 mg/kg. The 90-day rates of good outcome (modified Rankin Scale score ≤1) for the combined tenecteplase group was 39.1%, which was significantly higher than the 312 placebo patients (27.2%; 95% confidence interval, 0.031–0.209; P=0.0081) in the NINDS-TPA trial. We also found that the rates of symptomatic intracerebral hemorrhage were not statistically different between the tenecteplase group and the NINDS-TPA alteplase arm (3.2% versus 6.4%; 95% confidence interval, −0.075 to 0.011; P=0.146). These results are not corrected for potentially confounding variables, such as the initial National Institutes of Health Stroke Scale scores, age, and comorbidities. Indeed, the tenecteplase patients had lower median National Institutes of Health Stroke Scale scores on presentation than the placebo and alteplase arms of the NINDS-TPA trial. Nevertheless, our analysis combined with the growing evidence with respect to the efficacy of tenecteplase, signal a favorable prospect for reexamining the use of this drug in acute ischemic stroke.

Disclosures

None.

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References


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