Thrombolysis may be effective up to 9 hours after stroke onset in some cases

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Thrombolysis appears to be effective up to 9 hours after stroke onset in certain patients with acute ischemic stroke.

Researchers for the EXTEND (Extending the Time for Thrombolysis in Emergency Neurological Deficits) trial randomly assigned patients from study sites in Australia, New Zealand, Taiwan, and Finland to receive IV alteplase or placebo between 4.5 and 9 hours after stroke onset or after awakening with a stroke, as long as they were within 9 hours from the midpoint of sleep. Patients were eligible for the study if they were 18 years of age or older, had excellent functional status before enrollment, had a clinical severity score of 4 to 26 on the National Institutes of Health Stroke Scale (NIHSS), and had hypoperfused but salvageable brain regions on automated perfusion imaging. The study's primary outcome was a modified Rankin scale score of 0 or 1 at 90 days, where 0 indicates no symptoms and 6 indicates death. The risk ratio for this outcome was adjusted for age and NIHSS score at baseline. Results were published May 9 by the *New England Journal of Medicine*.

One hundred thirteen patients were randomly assigned to the alteplase group, and 112 patients were randomly assigned to the placebo group. The trial initially planned to enroll 310 patients but was terminated after 225 patients were enrolled because positive results from an earlier trial were published and clinical equipoise was lost. The primary outcome was seen in 40 patients in the alteplase group and 33 patients in the placebo group (35.4% vs. 29.5%; adjusted risk ratio, 1.44 [95% CI, 1.01 to 2.06]; P=0.04). No significant difference

was seen in 90-day mortality between the two groups (13 patients vs. 10 patients [11.5% vs. 8.9%]; adjusted risk ratio, 1.17 [95% CI, 0.57 to 2.40]; *P*=0.67). Item added Seven patients in the alteplase group and one patient in the placebo group had a symptomatic intracerebral hemorrhage (6.2% vs. 0.9%; adjusted risk ratio, 7.22 [95% CI, 0.97 to 53.54]; *P*=0.053). The researchers performed a secondary ordinal analysis of the distribution of modified Rankin scale scores and found no significant between-group difference in functional improvement at 90 days.

The researchers noted that their trial was terminated at 73% of the planned sample size and that they did not find a significant difference in functional improvement between groups. In addition, among other limitations, they pointed out that while the adjusted analyses found between-group differences in primary and secondary outcomes, the unadjusted analyses did not. They concluded, however, that alteplase therapy between 4.5 and 9 hours after stroke onset or awakening with stroke symptoms in patients who had a favorable perfusion profile was more likely to result in no or minor neurologic deficits versus placebo.

“Because of the limited power of our conclusions as a result of premature termination of the trial and the lack of a significant between-group difference in the secondary outcome of functional improvement, further trials of thrombolysis in this time window are required,” the authors wrote.