American Heart Association | American Stroke Association

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Top Ten Things To Know
Modern Evidence for the Inclusion and Exclusion Criteria for IV Alteplase in AIS

1. IV alteplase (recombinant tissue plasminogen activator) remains the only FDA approved (1996) medication proven for positive outcomes when given in the hyperacute time window in acute ischemic stroke (AIS).

2. The most common reason for not treating with alteplase is due to delays in presentation to medical attention (only 22-31% of AIS patients present to the Emergency Department within 3 hours of symptom onset).

3. Thrombolysis science is evolving with a defined and growing literature on the indications, benefits and risks associated with alteplase not available at the time of the early design of the original alteplase trials for AIS.

4. Current inclusion/exclusion criteria are based on the original NIH NINDS alteplase pilot studies, and many came from the cardiac literature (cardiac thrombolysis trials).

5. The purpose of this paper is to critically examine and review the evidence for the inclusion and exclusion criteria for IV alteplase in AIS. By doing so, this will help inform stroke care providers of the quantitative and the qualitative risks with the administration of IV alteplase.

6. This statement discusses the following inclusion/exclusion criteria: age issues (children and elderly), stroke severity and the NIHSS, rapidly improving symptoms, time from symptom onset, acute ICH on CT, pregnancy and postpartum, platelets, history of bleeding diathesis or coagulopathy, history of anticoagulant use, major surgery within 14 days, major trauma within 14 days and serious head trauma within 3 months, cardiac conditions, history of intracranial/spinal surgery within 3 months, history of ischemic stroke within 3 months, active internal bleeding or history of GI or GU bleeding within 21 days, arterial puncture or non-compressible vessels in the preceding 7 days, uncontrolled hypertension, severe hypertension repeated BP or requiring aggressive treatment, history of ICH, unruptured intracranial aneurysm, intracranial vascular malformation, intracranial neoplasms, serious medical comorbid illnesses, pre-existing disability, blood glucose, seizure at stroke onset syndrome, major early infarct size, large areas of ischemic stroke, early ischemic changes as measured by ASPECTS or 1/3rd rule, diabetic hemorrhage retinopathy or other ophthalmological conditions, suspicion of SAH on pretreatment evaluation, examining the individual exclusions to an extended time window from the ECASS-3 trial, and other topics.

7. Class and level of evidence assignments are made based on a modern evidence review for each exclusion discussed in this paper.

8. Future study is needed in the following areas: mild ischemic stroke, multimodal imaging techniques, international harmonization of administration criteria, persons who are anticoagulated (new agents), periprocedural or perioperative ischemic stroke, treatment with alteplase in persons with recent ischemic stroke, and treatment in persons with pre-existing disabilities and dementia.

9. After review of the literature, it is evident that supporting individual exclusion criteria vary widely. Clear evidence exists for benefit for several exclusion criteria such as: age (elderly) severe stroke, diabetes/hyperglycemia, and persons with minor early ischemic changes found on CT.

10. The information within this paper and the class and level of evidence assigned to each exclusion criteria help guide the clinician in decision making when considering hyperacute treatment with alteplase in the setting of AIS.

Demaerschalk et al; on behalf of the American Heart Association Stroke Council and Council on Epidemiology and Prevention. Scientific rationale for the inclusion and exclusion criteria for intravenous alteplase in acute ischemic stroke: a statement for healthcare professionals from the American Heart Association/American Stroke Association [published online ahead of print December 22, 2015]. Stroke. doi: 10.1161/STR.0000000000000086.