TPA Stroke Study Group Guidelines

Administration of rt-PA to Acute Ischemic Stroke Patients

1. Eligibility for IV treatment with rt-PA
   - Age 18 or older.
   - Clinical diagnosis of ischemic stroke causing a measurable neurological deficit.
   - Time of symptom onset well established to be less than 180 minutes before treatment would begin.

2. Patient Selection: Contraindications\(^C\) and Warnings\(^W\)
   - Evidence of intracranial hemorrhage on pretreatment CT.\(^C\)
   - Only minor or rapidly improving stroke symptoms.\(^W\)
   - Clinical presentation suggestive of subarachnoid hemorrhage, even with normal CT.\(^C\)
   - Active internal bleeding.\(^C\)
   - Known bleeding diathesis, including but not limited to:
     - Platelet count < 100,000/mm
     - Patient has received heparin within 48 hours and has an elevated aPTT (greater than upper limit of normal for laboratory)
     - Current use of oral anticoagulants (e.g., warfarin sodium) or recent use with an elevated prothrombin time > 15 seconds
   - Patient has had major surgery or serious trauma excluding head trauma in the previous 14 days.\(^W\)
   - Within 3 months any intracranial surgery, serious head trauma, or previous stroke.\(^C\)
   - History of gastrointestinal or urinary tract hemorrhage within 21 days.\(^W\)
   - Recent arterial puncture at a noncompressible site.\(^W\)
   - Recent lumbar puncture.\(^W\)
   - On repeated measurements, systolic blood pressure greater than 185 mm Hg or diastolic blood pressure greater than 110 mm Hg at the time treatment is to begin, and patient requires
aggressive treatment to reduce blood pressure to within these limits.\textsuperscript{c}
- History of intracranial hemorrhage.\textsuperscript{c}
- Abnormal blood glucose ( < 50 or > 400 mg/dL).\textsuperscript{w}
- Post myocardial infarction pericarditis.\textsuperscript{w}
- Patient was observed to have seizure at the same time the onset of stroke symptoms were observed.\textsuperscript{w}
- Known arteriovenous malformation, or aneurysm.\textsuperscript{c}

3. Treatment
- 0.9 mg/kg (maximum of 90 mg) infused over 60 minutes with 10\% of the total dose administered as an initial intravenous bolus over 1 minute.

4. Sequence of Events
- Determine whether time is available to start treatment with rt-PA before 3 hours.
- Draw blood for tests while preparations are made to perform non-contrast CT scan.
- Start recording blood pressure.
- Neurological examination.
- CT scan without contrast.
- Determine if CT has evidence of hemorrhage.
- If patient has severe head or neck pain, or is somnolent or stuporous, be sure there is no evidence of subarachnoid hemorrhage.
- If there is a significant abnormal lucency suggestive of infarction, reconsider the patient's history, since the stroke may have occurred earlier.
- Review required test results.
- Hematocrit.
- Platelets.
- Blood glucose.
- PT or aPTT (in patients with recent use of oral anticoagulants or heparin)
- Review patient selection criteria.
- Infuse rt-PA.
- Give 0.9 mg/kg, 10\% as a bolus, intravenously.
- Do not use the cardiac dose.
- Do not exceed the 90 mg maximum dose.
- Do not give aspirin, heparin or warfarin for 24 hours.
- Monitor the patient carefully, especially the blood pressure. Follow the blood pressure algorithm (see below and sample orders).
- Monitor neurological status. (see sample
orders).

5. Adjunctive Therapy
   - No concomitant heparin, warfarin, or aspirin during the first 24 hours after symptom onset. If heparin or any other anticoagulant is indicated after 24 hours, consider performing a non-contrast CT scan or other sensitive diagnostic imaging method to rule out any intracranial hemorrhage before starting an anticoagulant.

6. Blood Pressure Control
   - Pretreatment.
   - Monitor blood pressure every 15 minutes. It should be below 185/110 mm Hg.
   - If over 185/110, BP may be treated with nitroglycerin paste and/or one or two 10-20mg doses of labetalol given IV push within one hour. If these measures do not reduce BP below 185/110 and keep it down, the patient should not be treated with rt-PA.
   - During and after treatment.
   - Monitor blood pressure for the first 24 hours after starting treatment:
     - Every 15 minutes for 2 hours after starting the infusion, then
     - Every 30 minutes for 6 hours, then
     - Every hour for 18 hours.
   - If diastolic BP > 140 mm Hg, start an intravenous infusion of sodium nitroprusside (0.5 to 10 m g/kg/min).
   - If systolic BP > 230 mm Hg and/or diastolic BP is 121-140 mm Hg, give labetalol 20 mg intravenously over 1 to 2 minutes. The dose may be repeated and/or doubled every 10 minutes, up to 150 mg. Alternatively, following the first bolus of labetalol, an intravenous infusion of 2 to 8 mg/min labetalol may be initiated and continued until the desired BP is reached. If satisfactory response is not obtained, use sodium nitroprusside.
   - If systolic BP is 180 to 230 mm Hg and/or diastolic BP is 105 to 120 mm Hg on two readings 5 to 10 minutes apart, give labetalol 10 mg intravenously over 1 to 2 minutes. The dose may be repeated or doubled every 10 to 20 minutes, up to 150 mg. Alternatively, following the first bolus of labetalol, an intravenous infusion of 2 to 8 mg/min labetalol may be initiated and continued until the desired blood pressure is reached.
   - Monitor blood pressure every 15 minutes during the antihypertensive therapy. Observe
for hypotension.
- If, in the clinical judgment of the treating physician, an intracranial hemorrhage is suspected, the administration of rt-PA should be discontinued and an emergency CT scan or other diagnostic imaging method sensitive for the presence of intracranial hemorrhage should be obtained.

7. Management of Intracranial Hemorrhage (see also: intracranial hemorrhage algorithm)
- Suspect the occurrence of intracranial hemorrhage following the start of rt-PA infusion if there is any acute neurological deterioration, new headache, acute hypertension, or nausea and vomiting.
- If hemorrhage is suspected then do the following:
  - Discontinue rt-PA infusion unless other causes of neurological deterioration are apparent.
  - Immediate CT scan or other diagnostic imaging method sensitive for the presence of hemorrhage.
  - Draw blood for PT, aPTT, platelet count, fibrinogen, and type and cross (may wait to do actual type and cross).
  - Prepare for administration of 6 to 8 units of cryoprecipitate containing factor VIII.
  - Prepare for administration of 6 to 8 units of platelets.
- If intracranial hemorrhage present:
  - Obtain fibrinogen results.
  - Consider administering cryoprecipitate or platelets if needed.
  - Consider alerting and consulting a hematologist or neurosurgeon.
  - Consider decision regarding further medical and/or surgical therapy.
  - Consider second CT to assess progression of intracranial hemorrhage.
  - A plan for access to emergent neurosurgical consultation is highly recommended.

Notes

Note 1. This Protocol is Based on Research Supported by the National Institute of Neurological Disorders and Stroke (NINDS) (N01-NS-02382, N01-NS-02374, N01-NS-02377, N01-NS-02381, N01-NS-02379, N01-NS-02373, N01-NS-02378, N01-NS-02376, N01-NS-02380).

Note 2. Reference should also be made to the
manufacturer’s prescribing information for alteplase (Genentech Inc., South San Francisco, California).

Note 3. In patients without recent use of oral anticoagulants or heparin, treatment with rt-PA can be initiated prior to the availability of coagulation study results but should be discontinued if either the prothrombin time is greater than 15 seconds or the partial thromboplastin time is elevated by local laboratory standards.