

Memorial Hermann Health Stroke System and UTHealth Stroke Clinical Protocol for IV Alteplase

General Guidelines: In all cases, the anticipated benefit needs to be weighed against the risks, so that in the later time windows when benefit from IV Alteplase is less, or in the patient with minimal deficits who has less to gain from treatment with IV Alteplase, one should be more cautious with administration to patients who have an underlying clinical profile that might be associated with increased bleeding risk. All IV Alteplase administration referenced below is based on standard dosing (0.9mg/kg; 90mg max dose).

1. Thrombolytic treatment in patients presenting within 0-4.5 hours of symptom onset.

- a. IV Alteplase is recommended for patients who meet IV criteria and be treated within 4.5 hours of ischemic stroke symptom onset or patient last known well. (Stroke. 2019;50:e344–e418. Table 8).
 - i. Per AHA guidelines (Table 3.5.2 Time Windows; e363-Section 3.5.2) there is not published data that ECASS III exclusion criteria (age > 80, warfarin regardless of INR, combined history of diabetes and prior stroke, and NIHSS > 25) are justified in practice.

2. Thrombolytic Treatment in patients with unknown last seen normal, wake up strokes, and patients presenting beyond 4.5 hours from symptom onset.

- a. 4.5-9 hours
 - i. The EXTEND Trial showed benefit in treating patients IV Alteplase who demonstrate salvageable tissue on perfusion imaging between 4.5 to 9 hrs from last known well. CTP eligibility: <70 cc core volume and perfusion-ischemia mismatch ratio >1.2 (NEJM. 2019; 380:1795-1803).
 - ii. The WAKE-UP stroke trial demonstrated benefit of IV Alteplase in MRI-selected patients. Patients were treated within 4.5 hours of stroke symptom recognition if MRI demonstrated DWI-FLAIR mismatch (hyperintense DWI with normal FLAIR). (NEJM. 2018; 379:611-622).
- b. >9 hours
 - i. See 2aii above. The WAKE-UP trial enrolled patients with unknown LSN time.
- c. **Patients with proximal, large vessel occlusion (**LVO**) of terminal ICA or M1 MCA and a CT-perfusion target mismatch should concurrently be screened for endovascular therapy (**EVT**). See: Memorial Hermann Texas Medical Center- Endovascular Protocol for Acute Stroke Intervention.
- d. If no proximal anterior circulation LVO and MRI not feasible (patient characteristics such as pacemaker, unable to perform due to time-limitations, etc) can consider treatment if:
 - i. CT head (CTH) is normal, may obtain consent and proceed with treatment.
 - ii. If CTH shows less than 1/3 Middle Cerebral Artery (MCA) involvement (or equivalent in other territories) with a large vessel occlusion OR deficits appear out of proportion to ischemic area, may obtain consent and proceed with treatment.

iii. DO NOT TREAT IF ESTABLISHED HYPODENSITY COMPARED WITH ACUTE ISCHEMIC STROKE.

- e. If basilar artery thrombosis, proceed with treatment if patient's neurological examination is consistent with only partial involvement of the midbrain/pons. However if patient's examination is consistent with complete involvement of the brainstem, consider STAT MRI (DWI, FLAIR, GRE) brain to assess for degree of infarct, then proceed with treatment depending upon imaging results.
- f. Obtain Consent as per above.

3. Stroke and Myocardial infarction from 1 week to 3 months from onset of acute stroke symptoms (concerning for myocardial wall rupture)

- a. For patients presenting with concurrent acute ischemic stroke and acute MI, treatment with intravenous Alteplase at the dose appropriate for cerebral ischemia, followed by percutaneous coronary angioplasty and stenting if indicated, is reasonable (class IIa; Level of Evidence c).
- b. For patients presenting with acute ischemic stroke and a history of recent MI in the past 3 months, treating the ischemic stroke with intravenous Alteplase is reasonable if the recent MI was non-STEMI (*Class IIa; Level of Evidence C*), is reasonable if the recent MI was STEMI involving the right or inferior myocardium (*Class IIa; Level of Evidence C*), and may be reasonable if the recent MI was STEMI involving the left anterior myocardium
- c. If Q waves present, STAT Echo to assess the left ventricular wall morphology. If no evidence of myocardial wall thinning or pericardial effusion greater than the normal limit, then proceed with treatment. If not Q waves may be treated.

4. Stroke and Myocardial infarction within the last week from onset of acute stroke symptoms (concerning for myocardial wall rupture and hemopericardium w/ Alteplase)

- a. Check EKG for any evidence of pericarditis (diffuse ST-segment elevations). If patient is hypotensive or has positive JVD then do not treat. If evidence of pericarditis present then do not give Alteplase due to risk of hemopericardium.
- b. If N-STEMI- treat with Alteplase.
- c. If Q wave STEMI, obtain echo to evaluate myocardial wall for thinning or pericardial effusion. If no thinning or pericardial effusion greater than the normal limit present then proceed with treatment.
- d. If non- Q wave STEMI, may be treated.
- e. Consider Cardiology consult.

5. Pericarditis

- a. For patients with major acute ischemic stroke likely to produce severe disability and acute pericarditis, treatment with intravenous Alteplase may be reasonable (*Class IIb; Level of Evidence C*); urgent consultation with a cardiologist is recommended in this situation.
- b. For patients presenting with moderate acute ischemic stroke likely to produce mild disability and acute pericarditis, treatment with intravenous Alteplase is of uncertain net benefit (*Class IIb; Level of Evidence C*).

6. Left sided heart thrombus

- a. For patients with major acute ischemic stroke likely to produce severe disability and known left atrial or ventricular thrombus, treatment with intravenous Alteplase may be reasonable (*Class IIb; Level of Evidence C*).
- b. For patients presenting with moderate acute ischemic stroke likely to produce mild disability and known left atrial or ventricular thrombus, treatment with intravenous Alteplase is of uncertain net benefit (*Class IIb; Level of Evidence C*).

7. Endocarditis

- a. For patients with acute ischemic stroke and symptoms consistent with infective endocarditis, treatment with intravenous Alteplase is not recommended because of the increased risk of intracranial hemorrhage (*Class III; Level of Evidence C*).

8. Intracardiac mass

- a. For patients with major acute ischemic stroke likely to produce severe disability and cardiac myxoma, treatment with intravenous Alteplase may be reasonable (*Class IIb; Level of Evidence C*).
- b. For patients presenting with major acute ischemic stroke likely to produce severe disability and papillary fibroelastoma, treatment with intravenous Alteplase may be reasonable (*Class IIb; Level of Evidence C*).

9. Surgery within the last two weeks

- a. Depending on surgery, concern for bleeding needs to be weighed against disabling symptoms of stroke and that patients can be transfused; can obtain a stat consult of the respective surgical service.
- b. Recommend Alteplase for knee/hip replacement.

10. Recent Ischemic stroke

- a. For Stroke within prior 3 weeks: do not give Alteplase
- b. For Stroke: within the last 3 weeks-3 months, our practice is that treatment is reasonable if no edema or blood on CT. Consider Contrast CT or MRI to see if any evidence of BBB breakdown. One study from SITS registry found Alteplase to be safe when given within 3 months of prior stroke (Stroke. 2015 Nov;46(11):3184).

11. Cranial/spinal surgery within the last 3 months

- a. Obtain a stat neurosurgery consult.
- b. For patients with acute ischemic stroke and a history of intracranial/spinal surgery within the prior 3 months, intravenous Alteplase is potentially harmful (*Class III; Level of Evidence C*).
- c. Dr. Day's input: if the deficits are disabling, can consider IV ALTEPLASE if the surgery took place at least 1 week prior to acute stroke and as long as the original surgery was uncomplicated. If there was some sort of vascular injury from the procedure, do not treat with IV Alteplase. A good quality CT scan must exclude blood.
- d. Do not treat with IV Alteplase if surgical resection of a parenchymal tumor, vascular lesion including AVMs, or hemorrhage.

12. Major Trauma within 14 days

- a. In acute ischemic stroke patients with recent major trauma (within 14 days), intravenous Alteplase may be carefully considered, with the risks of bleeding from injuries related to the trauma weighed against the severity and potential disability from the ischemic stroke (*Class IIb; Level of Evidence C*).

13. Severe head trauma within 3 months

- a. In acute ischemic stroke patients with recent severe head trauma (within 3 months), intravenous Alteplase is contraindicated (*Class III; Level of Evidence C*).
- b. Given the possibility of bleeding complications from the underlying severe head trauma, intravenous Alteplase is not recommended in posttraumatic infarction that occurs during the acute in-hospital phase (*Class III; Level of Evidence C*).

14. Mild TBI/Concussion

- a. Do not treat with IV Alteplase if there was a concurrent head trauma at time of acute ischemic stroke.
- b. If head trauma occurred at least 3 weeks prior to acute ischemic stroke: can consider IV ALTEPLASE, as long as the original injury was uncomplicated by a SAH, ICH or IVH. If there was some sort of vascular injury of concern (i.e. SAH or contusion/ICH/IVH, do not treat with IV Alteplase. A good quality CT scan must exclude blood and there was no hemorrhage at time of the event to potentially qualify for Alteplase.
- c. A history of loss of consciousness that occurs in concussions in the absence of blood on CT, implies a functional disruption. Disabling deficits supersedes the risks of unexpected ALTEPLASE bleeding in these cases.

15. Gastrointestinal Hemorrhage

- a. If patient is having an active GI bleed as evidenced by history per patient/family, melena or bright red blood per rectum do not treat with IV Alteplase.
- b. AHA 2019 guidelines state IV Alteplase administration within 21 d of a GI bleeding event is not recommended. If patient has had a GI hemorrhage from unclear etiology which has required a blood transfusion in the last week, do not treat with IV Alteplase (*Stroke. 2019;50:e344–e418*).
- c. If considering IV Alteplase and the etiology of GI hemorrhage is confirmed, and patient did require blood transfusion, call GI stat to discuss if complications of another hemorrhage could be managed readily and easily to prevent detrimental blood loss.
- d. Patients with a structural GI malignancy are also considered high risk for IV Alteplase

16. Incidental unruptured and unsecured aneurysm

- a. Reasonable to treat
 - i. <10mm (*Class IIA, Level of Evidence C*)
- b. Consult neurosurgery
 - i. Large or Giant aneurysms. Risk and usefulness of Alteplase is unknown.

17. Intracranial neoplasms

- a. Extra-axial meningiomas- acceptable to treat.

- b. Pituitary Adenomas without evidence of hemorrhage on CT/MRI- ACCEPTABLE TO TREAT EXCEPT IN PREGNANCY.
- c. Intra-axial intracranial neoplasms
 - i. Do Not Treat

18. Pregnancy and Thrombolysis

- a. IV Alteplase does not cross the Placenta due to its molecular weight (Alteplase is 65kDa, and anything greater than 1kDa doesn't cross the placenta).
- b. After discussing the risk of possible fetal loss and obtaining consent from the patient, acceptable to treat.
- c. Consider IA as the initial treatment option, if available.
- d. The safety and efficacy of intravenous Alteplase in the early postpartum period (<14 days after delivery) have not been well established, consider urgent OB consultation

19. Acute Intracranial Hemorrhage on CT

- a. Intravenous Alteplase should not be administered to a patient whose CT reveals an acute intracranial hemorrhage (*Class III; Level of Evidence C*).

20. Platelets and Coagulation Studies

- a. The safety and efficacy of intravenous Alteplase for acute stroke patients with platelets <100 000/mm³, INR >1.7, aPTT >40 seconds, or PT >15 seconds are unknown, and intravenous Alteplase is not recommended (*Class III; Level of Evidence C*).
- b. If the PT is >15 but the INR is within normal limits, it is reasonable to treat with intravenous Alteplase.
- c. Given the extremely low risk of unsuspected abnormal platelet counts or coagulation studies in a population, it is reasonable that urgent intravenous Alteplase treatment not be delayed while waiting for hematologic or coagulation testing if there is no reason to suspect an abnormal test (*Class IIa; Level of Evidence B*).

21. History of bleeding diathesis/coagulopathy (Renal/Liver Failure)

- a. The safety and efficacy of intravenous Alteplase for acute stroke patients with a clinical history of potential bleeding diathesis or coagulopathy are unknown. Intravenous Alteplase may be considered on a case-by-case basis (*Class IIb; Level of Evidence C*).

22. Anticoagulant Use

- a. Intravenous Alteplase may be reasonable in patients who have a history of warfarin use and an INR ≤1.7 (*Class IIb; Level of Evidence B*).
- b. Intravenous Alteplase in patients who have a history of warfarin use and an INR >1.7 is not recommended (*Class III; Level of Evidence B*).
- c. Intravenous Alteplase should not be given to a patient who received heparin in the last 12 hours unless aPTT is normal. When patients have a stroke during or immediately after dialysis and received heparin during dialysis, heparin during dialysis is dosed so anticoagulant effect should be gone by the end of the procedure. However, in these cases, get aPTT first before deciding on Alteplase treatment.

- d. Intravenous Alteplase in patients who have received a dose of LMWH within the previous 24 hours is not recommended. This applies to both prophylactic doses and treatment doses (*Class III; Level of Evidence B*).
- e. The use of intravenous Alteplase in patients taking direct thrombin inhibitors or direct factor Xa inhibitors has not been firmly established but may be harmful (*Class III; Level of Evidence C*). The use of intravenous Alteplase in patients taking direct thrombin inhibitors or direct factor Xa inhibitors is not recommended unless laboratory tests such as aPTT, INR, platelet count, ecarin clotting time, thrombin time, or appropriate direct factor Xa activity assays (for rivaroxaban, apixaban, edoxaban), are normal or the patient has not received a dose of these agents for >48 hours (assuming normal renal metabolizing function).
- f. Dabigatran: If last dose was less than 48 hours and PTT, INR are normal, consider IV Alteplase with consent. It is reasonable to give Idarucizumab to reverse dabigatran, and then treat with Alteplase if aPTT is normal.
- g. Xa Inhibitor: If last dose was less than 48 hours, obtain TEG or Rapid TEG if possible. If R and/or ACT is normal, consider IV Alteplase with consent. It may be reasonable to give Andexanet A to reverse Xa inhibitors, and then treat with Alteplase if TEG is normal, but there is no experience with this to date.

23. Arterial Puncture of noncompressible vessels in the preceding 7 days

- a. The safety and efficacy of administering intravenous Alteplase to acute stroke patients who have had an arterial puncture of a noncompressible blood vessel in the 7 days preceding stroke symptoms are uncertain (*Class IIb; Level of Evidence C*).

24. Uncontrolled Hypertension, severe hypertension, repeated blood pressure or requiring aggressive treatment

- a. Intravenous Alteplase is recommended in patients whose blood pressure can be lowered safely (to <185/110 mm Hg) with antihypertensive agents, with the physician assessing the stability of the blood pressure before starting intravenous Alteplase (*Class I; Level of Evidence B*).
- b. If medications are given to lower blood pressure, the clinician should be sure that the blood pressure is stabilized at the lower level before beginning treatment with intravenous Alteplase and maintained below 180/105 mm Hg for at least the first 24 hours after intravenous Alteplase treatment (*Class I; Level of Evidence B*).

25. History of intracranial hemorrhage

- a. Cerebral Microbleeds (CMB): A high CMB burden (> 10 CMB) has been shown in multiple studies to be associated with increased risk for symptomatic ICH in Alteplase treated patients. Overall, intravenous alteplase in patients with CMBs is considered reasonable (*Class IIa; Level of Evidence B*). However, the risk/benefit ratio of intravenous Alteplase administration in patients with >10 CMBs should be carefully considered.
- b. Intravenous Alteplase administration in patients who have a history of intracranial hemorrhage is potentially harmful (*Class III; Level of Evidence C*).
- c. May consider Alteplase in specific instances: e.g, in a patient with a remote SAH where the aneurysm has been clipped, or a remote post traumatic bleed, or a remote infarct/surgery/CVT

where a hematoma occurred as a secondary complication, etc. However, would not administer Alteplase in patients with a prior hypertensive bleed; only exception to consider Alteplase for a hypertensive bleed is if the ICH was remote, other underlying causes of bleeding were excluded, and BP has been well controlled.

26. Intracranial vascular malformations

- a. For patients presenting with acute ischemic stroke who are known to harbor an unruptured and untreated intracranial vascular malformation, the usefulness and risks of administration of intravenous Alteplase are not well established (*Class IIb; Level of Evidence C*).
- b. Because of the increased risk of ICH in this population of patients, intravenous Alteplase may be considered in patients with stroke with severe neurologic deficits and a high likelihood of morbidity and mortality to outweigh the anticipated risk of ICH secondary to thrombolysis (*Class IIb; Level of Evidence C*).

27. Serious medical comorbid illnesses

- a. In patients with end-stage renal disease on hemodialysis and normal aPTT, intravenous Alteplase is recommended (*Class I; Level of Evidence C*). However, those with elevated aPTT may have elevated risk for hemorrhagic complications.
- b. Patients with preexisting dementia may benefit from intravenous Alteplase (*Class IIb; Level of Evidence B*). Individual considerations such as life expectancy and premorbid level of function are important to determine whether Alteplase may offer a clinically meaningful benefit.
- c. The safety and efficacy of Alteplase in patients with current malignancy are not well established (*Class IIb; Level of Evidence C*). Patients with systemic malignancy and reasonable (>6 months) life expectancy may benefit from intravenous Alteplase if other contraindications such as coagulation abnormalities, recent surgery, or systemic bleeding do not coexist.

28. Preexisting disability

- a. Preexisting disability does not seem to independently increase the risk of sICH after intravenous Alteplase, but it may be associated with less neurological improvement and higher mortality. Thrombolytic therapy with intravenous Alteplase for acute stroke patients with preexisting disability (mRS score ≥ 2) may be reasonable, but decisions should take into account relevant factors other than mRS (including quality of life, social support, place of residence, need for a caregiver after Alteplase administration, patients' and families' preferences, and goals of care) (*Class IIb; Level of Evidence B*).

29. Age Issues

- a. For otherwise medically eligible patients ≥ 18 years of age, intravenous Alteplase administration within 3 hours is equally recommended for patients < 80 and > 80 years of age. Older age is an adverse prognostic factor in stroke but does not modify the treatment effect of thrombolysis. Although older patients have poorer outcomes, higher mortality, and higher rates of sICH than those < 80 years of age, compared with control subjects, intravenous Alteplase provides a better chance of being independent at 3 months across all age groups.
- b. For patients presenting 0-4.5 hours- see section 1 A above.

30. Stroke Severity

- a. For severe stroke symptoms, intravenous Alteplase is indicated within 4.5 hours from symptom onset of ischemic stroke. Despite increased risk of hemorrhagic transformation, there is still proven clinical benefit for patients with severe stroke symptoms (*Class I; Level of Evidence A*).
- b. For patients with mild but disabling stroke symptoms, intravenous Alteplase is indicated within 4.5 hours from symptom onset of ischemic stroke. There should be no exclusion for patients with mild but nonetheless disabling stroke symptoms in the opinion of the treating physician from treatment with intravenous Alteplase because there is proven clinical benefit for those patients (*Class I; Level of Evidence A*).
- c. Within 4.5 hours from symptom onset, treatment of patients with milder ischemic stroke symptoms that are judged as nondisabling may be considered. Treatment risks should be weighed against possible benefits (***Class IIb; Level of Evidence C***).

31. Rapidly Improving symptoms

- a. Intravenous Alteplase treatment is reasonable for patients who present with moderate to severe ischemic stroke and demonstrate early improvement but remain moderately impaired and potentially disabled in the judgment of the examiner (*Class IIa; Level of Evidence A*).
- b. Because time from onset of symptoms to treatment has such a powerful impact on outcome, delaying treatment with intravenous Alteplase to monitor for further improvement is not recommended (*Class III; Level of Evidence C*).

32. Blood glucose

- a. Intravenous Alteplase is recommended in otherwise eligible patients within initial glucose levels >50 mg/ dL (*Class I; Level of Evidence A*).
- b. Treating clinicians should be aware that hypoglycemia and hyperglycemia may mimic acute stroke presentations and check blood glucose levels before intravenous initiation. Intravenous Alteplase is not indicated for nonvascular conditions (*Class III; Level of Evidence B*).
- c. Treatment with intravenous Alteplase in patients with acute ischemic stroke who present with initial glucose levels >400 mg/dL that are subsequently normalized and who are otherwise eligible may be reasonable (*Class IIb; Level of Evidence C*). However, there is no evidence that hyperglycemia must be corrected prior to Alteplase treatment.

33. Seizure at stroke onset

- a. Intravenous Alteplase is reasonable in patients with a seizure at the time of onset of acute stroke if evidence suggests that residual impairments are secondary to stroke and not a postictal phenomenon (*Class IIa; Level of Evidence C*).

34. Early ischemic changes on CT

- a. Intravenous Alteplase administration is recommended in the setting of EICs of mild to moderate extent (other than frank hypodensity) (*Class I; Level of Evidence A*).
- b. There remains insufficient evidence to identify a threshold of hypoattenuation severity or extent that affects treatment response to Alteplase. However, administering intravenous Alteplase to patients whose CT brain imaging exhibits extensive regions of clear

hypoattenuation is not recommended. These patients have a poor prognosis despite intravenous Alteplase, and severe hypoattenuation defined as obvious hypodensity represents irreversible injury (*Class III; Level of Evidence A*).

35. Diabetic hemorrhagic retinopathy or other hemorrhagic ophthalmological conditions

- a. Use of intravenous Alteplase in patients presenting with acute ischemic stroke who have a history of diabetic hemorrhagic retinopathy or other hemorrhagic ophthalmic conditions is reasonable to recommend, but the potential increased risk of visual loss should be weighed against the anticipated benefits of reduced stroke-related neurological deficits (*Class IIa; Level of Evidence B*).

36. Suspicion of SAH on pretreatment evaluation

- a. Intravenous Alteplase is contraindicated in patients presenting with symptoms and signs most consistent with an SAH (*Class III; Level of Evidence C*).

37. Menstruation and menorrhagia

- a. Intravenous Alteplase is probably indicated in women who are menstruating who present with acute ischemic stroke and do not have a history of menorrhagia. However, women should be warned that Alteplase treatment could increase the degree of menstrual flow (*Class IIa; Level of Evidence C*).
- b. Because the potential benefits of intravenous Alteplase probably outweigh the risks of serious bleeding in patients with recent or active history of menorrhagia without clinically significant anemia or hypotension, intravenous Alteplase administration may be considered (*Class IIb; Level of Evidence C*).
- c. When there is a history of recent or active vaginal bleeding causing clinically significant anemia, then emergent consultation with a gynecologist is probably indicated before a decision about intravenous Alteplase is made (*Class IIa; Level of Evidence C*).
- d. In patients who are menstruating or have active vaginal bleeding and are treated with Alteplase, the degree of vaginal bleeding should be monitored for 24 hours after Alteplase (*Class I; Level of Evidence C*).

38. Aortic arch dissection and cervicocephalic arterial dissection, known or suspected

- a. Intravenous Alteplase in acute ischemic stroke known or suspected to be associated with acute aortic arch dissection is not recommended and is potentially harmful (*Class III; Level of Evidence C*). Risk is unknown in patients with chronic aortic dissection.
- b. Intravenous Alteplase in acute ischemic stroke known or suspected to be associated with extracranial cervical arterial dissection is reasonably safe within 4.5 hours and is probably recommended (*Class IIa; Level of Evidence C*).
- c. Intravenous Alteplase usefulness and hemorrhagic risk in acute ischemic stroke known or suspected to be associated with intracranial arterial dissection remain unknown, uncertain, and not well established (*Class IIb; Level of Evidence C*). If considering Alteplase, it is important to be sure that there is no SAH on CT.

39. Dural puncture within 7 days

- a. Intravenous Alteplase may be considered for patients who present with acute ischemic stroke, even in instances when they may have undergone a lumbar dural puncture in the preceding 7 days (Class IIb; Level of Evidence C).

40. Psychogenic/conversion/malingering/stroke mimic

- a. The risk of symptomatic intracranial hemorrhage in the SM population is quite low; thus, starting intravenous Alteplase is probably recommended in preference over delaying treatment to pursue additional diagnostic studies

41. Catheterization Laboratory Environment/ Endovascular Complications/Stroke Syndrome

- a. Intravenous Alteplase is reasonable for the treatment of acute ischemic stroke complications of cardiac or cerebral angiographic procedures, depending on the usual eligibility criteria

42. Consent for the incompetent patient

- a. In an emergency, when the patient is not competent and there is no immediately available legally authorized representative to provide proxy consent, it is recommended to proceed with intravenous Alteplase in an otherwise eligible patient with acute ischemic stroke (*Class I; Level of Evidence C*).
- b. Visual displays that convey the benefits and the risks of intravenous Alteplase can be useful to assist with shared decision making and aid in establishing informed consent (*Class IIa; Level of Evidence B*).

43. Concurrent antiplatelet medication

- a. The administration of aspirin (or other antiplatelet agents) as an adjunctive therapy within 24 hours of intravenous Alteplase is not recommended (*Class III; Level of Evidence C*).
- b. The concurrent administration of other intravenous antiplatelet agents that inhibit the glycoprotein IIb/ IIIa receptor is not recommended outside a clinical trial (*Class III; Level of Evidence B*).
- c. Intravenous Alteplase is recommended for patients taking antiplatelet drug monotherapy before stroke on the basis of evidence that the benefit of Alteplase outweighs a possible small increased risk of sICH (*Class I; Level of Evidence A*).
- d. Intravenous Alteplase is recommended for patients taking antiplatelet drug combination therapy (eg. aspirin and clopidogrel) before stroke on the basis of evidence that the benefit of Alteplase outweighs a probable increased risk of sICH (*Class I; Level of Evidence B*).

44. Drug use

- a. Treating clinicians should be aware that illicit drug use may be a contributing factor to incident stroke. Intravenous Alteplase is reasonable in instances of illicit drug use–associated acute ischemic stroke in patients with no other exclusions (*Class IIa; Level of Evidence C*).

45. Sickle Cell disease

- a. Acute management of ischemic stroke resulting from SCD should include optimal hydration, correction of hypoxemia, correction of systemic hypotension, and blood exchange to reduce the percentage of hemoglobin S levels (*Class I; Level of Evidence B*).
- b. Consult hematology.
- c. Intravenous Alteplase for adults presenting with an acute ischemic stroke with known SCD can be beneficial (*Class IIa; Stroke. 2019;50:e344–e418*).