Ischemic Stroke Studies

• **ADAPT** – registry of thrombectomy using first-pass aspiration technique
• **POINT** – ASA and Clopidogrel vs ASA and placebo in acute minor ischemic stroke or TIA
• **POSITIVE** – ineligible for tPA, randomize to thrombectomy or best medical therapy
• **Separator 3D** – refractory/ineglible for tPA, randomize to thrombectomy with Penumbra System, or Penumbra System with Separator 3D
• **SHINE** – Blood glucose control in acute ischemic stroke
• **SOCRATES** – Ticagrelor vs (ASA) in Patients with acute minor ischemic stroke or TIA
• **THERAPY** – randomize to tPA alone or tPA+thrombectomy
Hemorrhagic Studies

- **ACE** – registry of aneurysm coils
- **Acetaminophen for aSAH** – post-coiling drug study: acetaminophen for vasospasm
- **ATACH II** – BP control in acute ICH patients
- **CLEAR III** – tPA for IVH
- **FEAT** – randomize to 18 or standard framing coils for aneurysm treatment
ACE Inclusion Criteria

✓ Patient presents with an intracranial aneurysm, other neurovascular abnormality (AVM, AVF)
✓ Patient requires arterial and/or venous embolization in the peripheral vasculature
Patients in whom endovascular embolization therapies other than Penumbra Coils are used will be excluded from this study. However, adjunctive use of balloon and stent are acceptable.
Acetaminophen for aSAH
Inclusion Criteria

- Ages ≥ 20
- Fisher Grade III or III + IV SAH based upon admitting CT scan
- Aneurysm secured by either clipping or coiling within 72 hours of SAH
- Intracranial aneurysm confirmed by angiography or CTA
- Presence of ventriculostomy for external ventricular drainage (EVD) prior to randomization
Acetaminophen for aSAH

Exclusion Criteria

× Consent unobtainable
× Enrollment in another interventional study
× Patient is pregnant or lactating
× Known co-morbidities that could affect outcome of this study
× Contraindication to CTA
× Serum creatinine > 1.4
× Documented allergy to iodinated contrast that cannot be adequately treated with premedication
× Documented allergy and/or intolerance to ApAP
× Baseline liver disease
× History of recent alcohol abuse with documented ALT or AST above normal laboratory values
× Documented history of both malnutrition and decreased serum albumin below normal lab values
× Documented abnormal platelet count below normal lab values
× Documented abnormal PT or PTT above normal lab values
× Active asthma or chronic treatment to prevent asthma in the past year-this does not include exercise-induced asthma
× Documented allergy and/or intolerance to N-acetylcysteine
× Currently taking phenytoin, carbamazepine, or phenobarbital
× Currently taking isoniazid (INH, Lanzid, Nydrazid)
× Severe life-threatening complications resulting from standard aneurysm treatments that will likely prevent completion of the study
× Patient unsuitable for the study, in the opinion of the investigator(s)
ATACH II Inclusion Criteria

- Age 18 years or older
- IV nicardipine can be initiated within 4.5 hours of symptom onset
- Patient can be randomized within 4.5 hours of symptom onset
- Clinical signs consistent with the diagnosis of stroke, including impairment of language, motor function, cognition, and/or gaze, vision, or neglect
- Total GCS score (aggregate of verbal, eye, & motor response scores) of 5 or greater at ED arrival.
- INR value <1.5
- CT scan demonstrates intraparenchymal hematoma with manual hematoma volume measurement < 60cc
- For subjects randomized prior to IV antihypertensive administration: SBP greater than 180 mmHg* prior to IV antihypertensive treatment (this includes pre-hospital treatment) AND WITHOUT spontaneous SBP reduction to below 180mmHg at the time of randomization.
  OR
  For subjects randomized after IV antihypertensive administration: SBP greater than 180 prior to IV antihypertensive treatment (this includes pre-hospital treatment) AND WITHOUT SBP reduction to below 140mmHg at the time of randomization.
- Informed consent obtained by subject, legally authorized representative, or next of kin.
ATACH II Exclusion Criteria

- ICH is due to previously known neoplasms, AVM, or aneurysms
- Intracerebral hematoma considered to be related to trauma
- ICH located in infratentorial regions such as pons or cerebellum
- IVH associated with intraparenchymal hemorrhage and blood completely fills one lateral ventricle or more than half of both ventricles
- Patient to receive immediate surgical evacuation
- Current pregnancy, parturition within previous 30 days or active lactation
- Use of dabigatran within the last 48 hours
- A platelet count less than 50,000 mm$^3$
- Known sensitivity to nicardipine
- Pre-morbid disability requiring assistance in ambulation or activities of daily living
- Subject’s living will precludes aggressive ICU management
- Subject is currently participating in another interventional clinical trial.
CLEAR III Inclusion Criteria

✓ Age 18-80.
✓ Symptom onset less than 24 hrs prior to diagnostic CT scan.
✓ Spontaneous ICH ≤ 30 cc and IVH obstructing 3rd and/or 4th ventricles.
✓ ICH clot stability: ICH must be ≤ 30 cc on initial presentation and not exceed 35 cc on subsequent pre-randomization stability scans.
✓ IVH clot stability: The width of the lateral ventricle most compromised by blood clot must not increase by > 2 mm, allowing for movement of blood under influence of gravity.
✓ Catheter tract bleeding must be less than or equal to 5 cc on CT scan for stability.
✓ On stability CT scan, the 3rd and/or 4th ventricles are occluded with blood.
✓ Standard of care EVD placement, done using no more than 2 complete passes (including “soft passes” using the original trajectory). *If >2 passes required, need additional sCT 24 hours post-EVD placement.
✓ Patients with primary IVH are eligible (i.e. with ICH=0).
✓ SBP < 200 mmHg sustained for 6h up to randomization/dosing.
✓ No test article may be administered until at least 12 hours after symptom onset.
✓ Able to randomize within 72 h of CT scan diagnosing IVH (provided the time of symptom onset to diagnostic CT does not exceed 24 h).
✓ Historical Rankin of 0 or 1.
CLEAR III Exclusion Criteria

× Suspected or untreated ruptured cerebral aneurysm, ruptured intracranial AVM, or tumor. Treatment of an existing aneurysm or AVM must have occurred at least 3 months before the current onset.

× Presence of a choroid plexus vascular malformation or Moyamoya disease.

× Clotting disorders.

× Platelet count < 100,000; INR > 1.4.

× Pregnancy (positive serum or urine pregnancy test).

× Infratentorial hemorrhage

× Thalamic bleeds with apparent midbrain extension that do not have third nerve palsy or do not exhibit dilated and non-reactive pupils are eligible for participation in the study. Patients with transient oculomotor dysfunction are eligible for participation. Note: Patients with a posterior fossa ICH or cerebellar hematomas are ineligible.

× SAH at clinical presentation – must obtain angiogram (angio, CTA, MRA/MRI) when the diagnostic CT scan shows SAH or any hematoma location or appearance not strongly associated with hypertension. If the angiogram or other imaging does not detect a bleeding source to account for the hemorrhage, the patient is eligible for the study.

× Ongoing internal bleeding, involving retroperitoneal sites, or the gastrointestinal, genitourinary, or respiratory tracts. (Patient with prior bleeding that is clinically stable for 12 h or more without any coagulopathy or bleeding disorder is eligible).

× Multi-focal, superficial bleeding, observed at multiple vascular puncture and access sites (e.g., venous cutdowns, arterial punctures) or site of recent surgical intervention.

× Prior enrollment in the study.

× Any other condition that the investigator believes would pose a significant hazard to the subject if the investigational therapy were initiated. Subjects who are not expected to survive to the day 180 visit due to comorbidities and/or are DNR/DNI status prior to randomization are excluded.

× Planned or simultaneous participation (between screening and Day-30) in another interventional medical investigation or clinical trial. Patients involved in observational, natural history, and/or epidemiological studies not involving an intervention are eligible.

× No subject or legal representative to give written informed consent.
FEAT Inclusion Criteria

- Patient presenting with ruptured or unruptured cerebral aneurysm appropriate for endovascular treatment as determined by the neurovascular treating team (neurointerventionist and/or neurosurgeon).
- The neurointerventionist feels that the aneurysm can be safely treated with either using, or not using, a 0.01-0.0155” platinum coil.
- Patients are at least 18 years old and less than 80 years of age.
- Patient must be Hunt and Hess grade 0 to 3.
- Patient has given fully informed consent to endovascular coiling procedure. If the patient cannot consent for themselves, appropriate written consent has been sought from their next of kin or appropriate power of attorney.
- Aneurysm 7-14 mm in maximum diameter.
- Patient is willing and able to return for clinical evaluation and follow-up imaging evaluation (angiography or MRA) at 3-6 months and 12-18 months after endovascular treatment.
- The patient has not been previously randomized into this trial or another conflicting/confounding trial.
- The aneurysm has not been previously treated by coiling or clipping.
FEAT Exclusion Criteria

× Patient has more than one aneurysm requiring treatment in the current treatment session, and only one of those to be treated aneurysms fits the FEAT inclusion criteria (ie - if either (1) a patient has multiple aneurysms, but only one will be treated at enrollment; or (2) if two or more aneurysms are treated during the current treatment session and BOTH are able to be enrolled, then they remain eligible for the trial). Non-treated additional aneurysms may be treated at a later date with any coil type that the operator chooses).

× Target aneurysm has had previous coil treatment or has been surgically clipped.

× Hunt and Hess score is 4 or 5 after subarachnoid hemorrhage.

× Inability to obtain informed consent.

× Medical or surgical co-morbidity such that the patient’s life expectancy is less than 2 years.
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ADAPT Inclusion Criteria

 ✓ All patients with acute stroke who are clinically treated with direct aspiration as a first pass choice or treated with a stent retriever will be included.
Patients not clinically treated with either direct aspiration as a first pass, or stent retriever will not be included.
POINT Inclusion Criteria

✓ Neurologic deficit (based on history or exam) attributed to focal brain ischemia and EITHER:
  • High risk TIA: Complete resolution of the deficit at the time of randomization AND ABCD2 score ≥4
  OR
  • Minor ischemic stroke: residual deficit with NIHSS ≤3 at the time of randomization.

✓ Ability to randomize within 12 hours of time last known free of new ischemic symptoms.

✓ Head CT or MRI ruling out hemorrhage or other pathology, such as vascular malformation, tumor, or abscess, that could explain symptoms or contraindicate therapy.

✓ Ability to tolerate aspirin at a dose of 50-325 mg/day.
POINT Exclusion Criteria

× Age <18 years.
× TIA symptoms limited to isolated numbness, isolated visual changes, or isolated dizziness/vertigo.
× In the judgement of the treating physician, a candidate for thrombolysis, endarterectomy or endovascular intervention, unless the subject declines both endarterectomy and endovascular intervention at the time of the evaluation for eligibility.
× Receipt of any intravenous or intra-arterial thrombolysis within 1 week prior to index event.
× Gastrointestinal bleed or major surgery within 3 months prior to index event.
× History of non-traumatic intracranial hemorrhage.
× Clear indication for anticoagulation (e.g., warfarin, heparin) anticipated during the study period (atrial fibrillation, mechanical heart valve, deep venous thrombosis, pulmonary embolism, antiphospholipid antibody syndrome, hypercoagulable state).
× Qualifying ischemic event induced by angiography or surgery.
× Severe non-cardiovascular comorbidity with life expectancy <3 months.
× Contraindication to clopidogrel or aspirin:
  – Known allergy
  – Severe renal (serum creatinine >2mg/dL or 178.6umol/L) or hepatic insufficiency (prior or concurrent diagnosis, with INR>1.5, or any resultant complication, such as variceal bleeding, encephalopathy, or icterus)
  – History of drug-induced hematologic or hepatic abnormalities
× Anticipated requirement for long term (>7 days) non-study antiplatelet drugs (eg, dipyridamole, clopidogrel, ticlopidine), or NSAIDs affecting platelet function (such as prior vascular stent or arthritis).
× Not willing or able to discontinue prohibited concomitant medications.
× Inability to swallow medications.
× At risk for pregnancy: premenopausal or postmenopausal woman within 12 months of last menses without a negative pregnancy test or not committing to adequate birth control (e.g., oral contraceptive, two methods of barrier birth control, or abstinence).
× Unavailability for follow-up.
× Signed and dated informed consent not obtained from patient.
× Other neurological conditions that would complicate assessment of outcomes during follow-up.
× Ongoing treatment in another study of an investigational therapy, or treatment in such a study within the last 7 days.
× Previously enrolled in the POINT study.
POSITIVE Inclusion Criteria

- Age 18 to 80 years (i.e., candidates must have had their 18th birthday, but not had their 81st birthday)
- NIHSS ≥8 at the time of neuroimaging
- Presenting or persistent symptoms within 12 hours of when groin puncture can be obtained
- Neuroimaging demonstrates large vessel proximal occlusion (distal ICA through MCA M1 bifurcation)
- The operator feels that the stroke can be appropriately treated with traditional endovascular techniques (endovascular mechanical thrombectomy without adjunctive devices such as stents)
- Pre-event Modified Rankin Scale score 0-1
- Consenting requirements met according to local IRB
POSITIVE Exclusion Criteria

- Patient is eligible for IV-tPA therapy
- Rapidly improving neurologic examination
- Absence of large vessel occlusion on non-invasive imaging
- Known or suspected pre-existing (chronic) large vessel occlusion in the symptomatic territory
- Absence of an associated large penumbra as defined by physiologic imaging according to standard of practice at the participating institution
- Any intracranial hemorrhage in the last 90 days
- Known irreversible bleeding disorder
- Known hereditary or acquired hemorrhagic diathesis, coagulation factor deficiency, or oral anticoagulant therapy with INR > 2.5 or institutionally equivalent prothrombin time of 2.5 times normal
- Platelet count < 100 x 10^3 cells/mm^3 or known platelet dysfunction
- Inability to tolerate, clinically documented evidence in medical history of adverse reaction to, or contraindication to medications used in treatment of the stroke
- Contraindication to CT and MRI (i.e., iodine contrast allergy or other condition that prohibits imaging from either CT or MRI)
- Known allergy to contrast used in angiography that cannot be medically controlled
- Relative contraindication to angiography (e.g., serum creatinine > 2.5 mg/dL)
- Women who are currently pregnant or breast-feeding (Women of childbearing potential must have a negative pregnancy test prior to the study procedure [either serum or urine])
- Evidence of active infection (indicated by fever at or over 99.9 °F and/or open draining wound) at the time of randomization
- Current use of cocaine or other vasoactive substance
- Any comorbid disease or condition expected to compromise survival or ability to complete follow-up assessments through 90 days
- Patients who lack the necessary mental capacity to participate or are unwilling or unable to comply with the protocol’s follow up appointment schedule (based on the investigator’s judgment)
- Current participation in another interventional (drug, device, etc.) research project

Head CT or MRI Scan Exclusion Criteria

- Presence of blood on imaging (subarachnoid hemorrhage (SAH), intracerebral hemorrhage (ICH), etc.)
- High density lesion consistent with hemorrhage of any degree
- Significant mass effect with midline shift
- Large (more than 1/3 of the middle cerebral artery) regions of clear hypodensity on the baseline CT scan or ASPECTS of < 7; Sulcal effacement and/or loss of grey-white differentiation alone are not contraindications for treatment.
Separator 3D Inclusion Criteria

- From 18 to 85 years of age
- Present with symptoms consistent with an acute ischemic stroke for revascularization within 8 hours from symptom onset
- Refractory to or not eligible for IV rtPA therapy, e.g., presenting between 0 and 3 hours from symptom onset AND contraindicated for IV rtPA, or presenting between 3 and 8 hours of symptom onset, or evidence of persistent occlusion from vascular imaging after IV rtPA
- Evidence of a large vessel (>2.5mm in diameter) occlusion in the cerebral circulation
- NIH Stroke Scale (NIHSS) score ≥8
- Signed informed consent
Separator 3D Exclusion Criteria

- History of stroke in the past 3 months.
- Females who are pregnant
- Pre-existing neurological or psychiatric disease that could confound the study results such as a pre-stroke mRS score >1
- Known severe allergy to contrast media
- Uncontrolled hypertension (defined as systolic blood pressure >185 mmHg or diastolic blood pressure >110 mmHg)
- CT evidence of the following conditions at randomization:
  - Significant mass effect with midline shift
  - Large infarct region >1/3 of the middle cerebral artery territory
  - Evidence of intracranial hemorrhage
- Angiographic evidence of an arterial stenosis proximal to the occlusion that could prevent thrombus removal
- Angiographic evidence of preexisting arterial injury
- Rapidly improving neurological status prior to enrollment
- Bilateral stroke
- Intracranial tumors
- Known history of cerebral aneurysm or arteriovenous malformation
- Known hemorrhagic diathesis, coagulation deficiency, or on anticoagulant therapy with an International Normalized Ratio (INR) of >1.7
- Baseline platelets <50,000
- Use of IV heparin in the past 48 hours with PTT >1.5 times the normalized ratio
- Baseline glucose <50mg/dL or >300mg/dL
- Life expectancy less than 90 days prior to stroke onset
- Participation in another clinical investigation that could confound the evaluation of the study device
SHINE Inclusion Criteria

✓ Age 18 years or older
✓ Clinical diagnosis of ischemic stroke defined as acute neurological deficit occurring in one or more cerebral vascular territories. Neuroimaging must be done to exclude intracranial hemorrhage (ICH).
✓ Protocol treatment must begin within 12 hours after stroke symptom onset and is recommended, but not required, to begin within 3 hours after hospital arrival. If time of symptom onset is unclear or patient is awakening with stroke symptoms, the time of onset will be the time the patient was last known to be normal.
✓ Known history of type 2 diabetes mellitus and glucose >110mg/dL OR admission glucose ≥150mg/dL in those w/o known diabetes mellitus
✓ Baseline NIHSS score of 3-22
✓ Pre-stroke modified Rankin Scale score=0 for patients with an NIHSS score of 3-7.
✓ Pre-stroke modified Rankin Scale score=0 or 1 for patients with an NIHSS score of 8-22.
✓ Able to provide a valid informed consent to be in the study (self or their authorized legally accepted representative). The approved consent form must be signed and dated in accordance with federal and institutional guidelines.
SHINE Exclusion Criteria

- Known history of type 1 diabetes mellitus
- Substantial pre-existing neurological or psychiatric illness that would confound the neurological assessment or other outcome assessment
- Having received experimental therapy for the enrollment stroke. IV tPA (up to 4.5 hrs) or IA tPA are allowed as are IA therapies including use of FDA cleared devices. Non FDA cleared devices are considered experimental and are excluded.
- Known to be pregnant or breast-feeding at the time of study entry
- Other serious conditions that make the patient unlikely to survive 90 days
- Inability to follow the protocol or return for the 90 day follow up
- Renal dialysis (including hemo or peritoneal dialysis)
SOCRATES Inclusion Criteria

✓ Provision of informed consent prior to any study specific procedures
✓ Men or women ≥40 years of age
✓ Either acute ischemic stroke or high-risk TIA as defined here and randomization occurring within 24 hours after onset of symptoms:
  – Acute ischemic stroke, defined as: Neurological deficit attributed to the focal brain ischemia, and either of the following:
    • Persistent signs or symptoms of the ischemic event at the time of randomization, OR
    • Acute, ischemic brain lesion documented by computed tomography scan or magnetic resonance imaging (diffusion-weighted imaging) within 24 hours of onset of symptoms.
    • National Institute of Health Stroke Score ≤5
  – High-risk TIA, defined as: Neurological deficit of acute onset attributed to focal ischemia of the brain by history or examination with complete resolution of the deficit, and at least one of the following:
    • ABCD2 score ≥4 and TIA symptoms not limited to isolated numbness, isolated visual changes, or isolated dizziness/vertigo
    • Symptomatic intracranial arterial occlusive disease documented by transcranial doppler ultrasound or vascular imaging, defined as at least 50% narrowing in diameter of a vessel that could account for the clinical presentation
    • Documented internal carotid arterial occlusive disease, defined as at least 50% narrowing in diameter of a vessel that could account for the clinical presentation
✓ Head Computed Tomography (CT) or MRI ruling out hemorrhage or other pathology, such as vascular malformation, tumor, or abscess that could explain symptoms or contraindicate therapy.
Planned use of antithrombotic therapy in addition to study medication including antiplatelets (eg, open label ASA, GPIIb/IIa inhibitors, clopidogrel, ticlopidine, prasugrel, dipyridamole, ozagrel, cilostazol) and anticoagulants (eg, warfarin, oral thrombin and factor Xa inhibitors, bivalirudin, hirudin, argatroban, unfractionated and low molecular weight heparins). In addition, patients receiving or requiring dual antiplatelet therapy with ASA and P2Y12 inhibitors will be excluded.

Known hypersensitivity to ticagrelor or ASA

Any history of atrial fibrillation, ventricular aneurysm or suspicion of cardioembolic pathology for TIA or stroke

Planned carotid, cerebrovascular, or coronary revascularisation that requires halting study medication within 7 days of randomisation

Receipt of any intravenous or intra-arterial thrombolysis or mechanical thrombectomy within 24 hours prior to randomisation

Anticipated concomitant oral or intravenous therapy with strong cytochrome P450 3A (CYP3A) inhibitors or CYP3A substrates with narrow therapeutic indices that cannot be stopped for the course of the study

- Strong inhibitors: ketoconazole, itraconazole, voriconazole, telithromycin, clarithromycin (but not erythromycin or azithromycin), nefazadone, ritonavir, saquinavir, nelfinavir, indinavir, atanazavir

- CYP3A substrates with narrow therapeutic index: cyclosporine, quinidine, simvastatin at doses >40 mg daily or lovastatin at doses >40 mg daily

Anticipated requirement for long-term (>7 days) non-steroidal anti-inflammatory drugs (NSAIDs)

Patients with known bleeding diathesis or coagulation disorder (eg, thrombotic thrombocytopenic purpura)

History of previous symptomatic non-traumatic intracerebral bleed at any time (asymptomatic microbleeds do not qualify), gastrointestinal (GI) bleed within the past 6 months, or major surgery within 30 days

Known severe liver disease (eg, ascites or signs of coagulopathy)

Renal failure requiring dialysis

Pregnancy or lactation

Involvement in the planning and/or conduct of the study (applies to both AstraZeneca staff and/or staff at the study site)

Inability of the patient to understand and/or comply with study procedures and/or follow-up, in the opinion of the Investigator

Previous enrolment or randomisation in the present study

Participation in another clinical study with an investigational product during the last 30 days
THERAPY Inclusion Criteria

- From 18 to 85 years of age
- Present with symptoms consistent with an acute ischemic stroke and eligible for IV rtPA therapy
- Evidence of a large vessel occlusion in the anterior circulation with a clot length of > 8mm
- NIH Stroke Scale (NIHSS) score > 8 or aphasic at presentation
- Signed informed consent
THERAPY Exclusion Criteria

- History of stroke in the past 3 months.
- Females who are pregnant
- Pre-existing neurological or psychiatric disease that could confound the study results such as a pre-stroke mRS score >1
- Known severe allergy to contrast media
- Uncontrolled hypertension (defined as systolic blood pressure >185 mmHg or diastolic blood pressure >110 mmHg)
- CT evidence of the following conditions at randomization:
  - Significant mass effect with midline shift
  - Large infarct region >1/3 of the middle cerebral artery territory
  - Evidence of intracranial hemorrhage
- Angiographic evidence of an arterial stenosis proximal to the occlusion that could prevent thrombus removal
- Angiographic evidence of preexisting arterial injury
- Rapidly improving neurological status prior to randomization
- Bilateral stroke
- Intracranial tumors
- Known history of cerebral aneurysm or arteriovenous malformation
- Known hemorrhagic diathesis, coagulation deficiency, or on anticoagulant therapy with an International Normalized Ratio (INR) of >1.7
- Baseline platelets <50,000
- Use of IV heparin in the past 48 hours with PPT >1.5 times the normalized ratio
- Baseline glucose <50mg/dL or >300mg/dL
- Life expectancy less than 90 days prior to stroke onset
- Participation in another clinical investigation that could confound the evaluation of the study device
1 – Jessi Marlin: 615-835-4018

**FEAT** – randomize to 18 or standard framing coils for aneurysm treatment

**POSITIVE** – randomize to thrombectomy or best medical therapy for patients ineligible for tPA
2 – Emily Gilchrist: 615-436-0434

ACE – registry of aneurysm coils
CLEAR III – tPA for IVH
ADAPT – registry of thrombectomy using first-pass aspiration technique
Separator 3D – refractory/ineglible for tPA, randomize to thrombectomy with Penumbra System, or Penumbra System with Separator 3D
3 – Diane Brown: 615-835-8151

**Acetaminophen for aSAH** – post-coiling drug study: acetaminophen for vasospasm

**ATACH II** – BP control in acute ICH patients

**POINT** – ASA and Clopidogrel vs ASA and placebo in acute minor ischemic stroke or TIA

**SHINE** – Blood glucose control in acute ischemic stroke

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