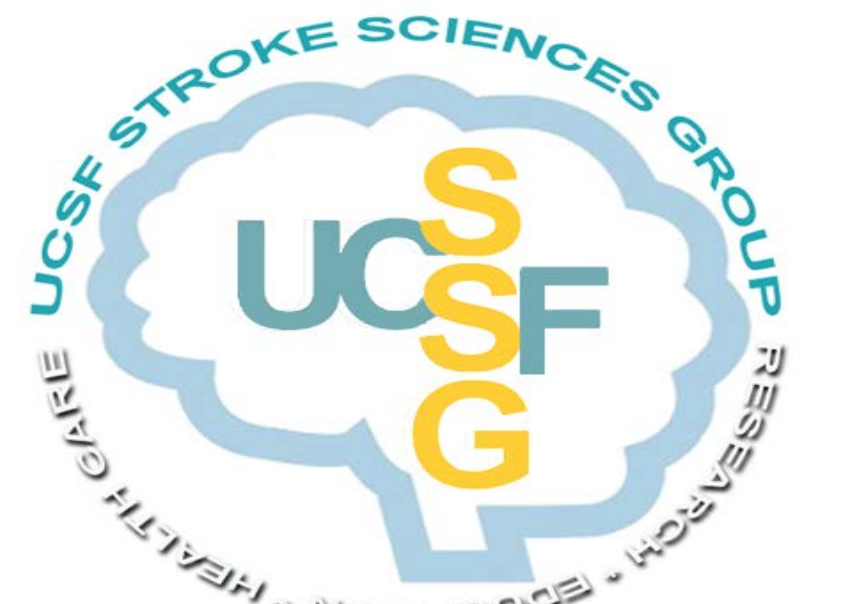




PLATELET-ORIENTED INHIBITION IN NEW TIA AND MINOR ISCHEMIC STROKE (POINT) TRIAL

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BACKGROUND

Transient ischemic attacks (TIAs) are *common* (over 250,000 diagnosed each year in the US) and *ominous*, with substantial short-term risk of stroke, hospitalization for cardiovascular events, and death. Attention has recently focused on TIA and the need for urgent evaluation and treatment. The CHANCE Trial suggests that aggressive treatment with antiplatelet therapy is effective, but results should be confirmed outside of China where treatment practices differ. POINT is designed to address the optimal antithrombotic treatment of acute TIA for prevention of secondary stroke.

PRIMARY OBJECTIVE

To determine whether clopidogrel 75mg/day after a loading dose of 600mg is effective in preventing major ischemic vascular events (ischemic stroke, myocardial infarction and ischemic vascular death) at 90 days when subjects are randomized within 12 hours of the time last known free of new ischemic symptoms in patients receiving aspirin 50-325mg/day.

STUDY DESIGN

A prospective, randomized, double-blind trial with the primary null hypothesis that in patients with TIA or minor ischemic stroke treated with aspirin 50-325mg/day, there is no difference in the event-free survival at 90 days in those treated with clopidogrel (600mg loading dose, then 75mg/day) compared to placebo, when randomization occurs within 12 hours of the time last known free of new ischemic symptoms. Each subject followed for 90 days from randomization.

PRIMARY ENDPOINT

Composite endpoint of new ischemic vascular events: ischemic stroke, myocardial infarction or ischemic vascular death at 90 days.

PATIENT POPULATION AND SAMPLE SIZE

Patients 18 years of age or older with high-risk TIA (defined as an ABCD² score ≥ 4) or minor ischemic stroke (NIHSS ≤ 3) who can be randomized within 12 hours of the time last known free of new ischemic symptoms will be enrolled. Total sample size for the study is 5,840 subjects enrolled at up to 250 US and international sites in partnership with the NINDS NETT and the POINT Clinical Research Collaboration (CRC).

INCLUSION CRITERIA

- Neurologic deficit (based on history/exam) attributed to focal brain ischemia, and **EITHER** **high-risk TIA** (complete resolution of deficit at time of randomization **AND** ABCD² score ≥ 4) **OR** **minor ischemic stroke** (residual deficit with NIHSS ≤ 3 at time of randomization)
- Randomization within 12 hours of time last known free of new ischemic symptoms
- Head CT or MRI ruling out hemorrhage/other pathology (e.g., tumor, abscess, vascular malformation) that could explain symptoms or contraindicate therapy
- Ability to tolerate aspirin at a dose of 50-325mg/day

EXCLUSION CRITERIA

- Age <18 years
- TIA symptoms limited to isolated numbness, visual changes, or dizziness/vertigo
- In the judgment of the treating physician, a candidate for thrombolysis, endarterectomy or endovascular intervention
- Receipt of intravenous or intra-arterial thrombolysis 1 week prior to index event
- Gastrointestinal bleed or major surgery within 3 months prior to index event
- History of nontraumatic intracranial hemorrhage
- Clear indication for anticoagulation (e.g., warfarin, heparin) anticipated during study period (e.g., atrial fibrillation, mechanical heart valve, DVT, 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
- Anticipated requirement for long-term (>7 days) non-study antiplatelet drugs (e.g., dipyridamole, 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: pre/post menopausal woman within 12 months of last menses without a negative pregnancy test or not committing to adequate birth control (oral contraceptive, 2 methods of barrier birth control, abstinence)
- Unavailability for follow-up
- Inability to provide written, signed and dated informed consent
- 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

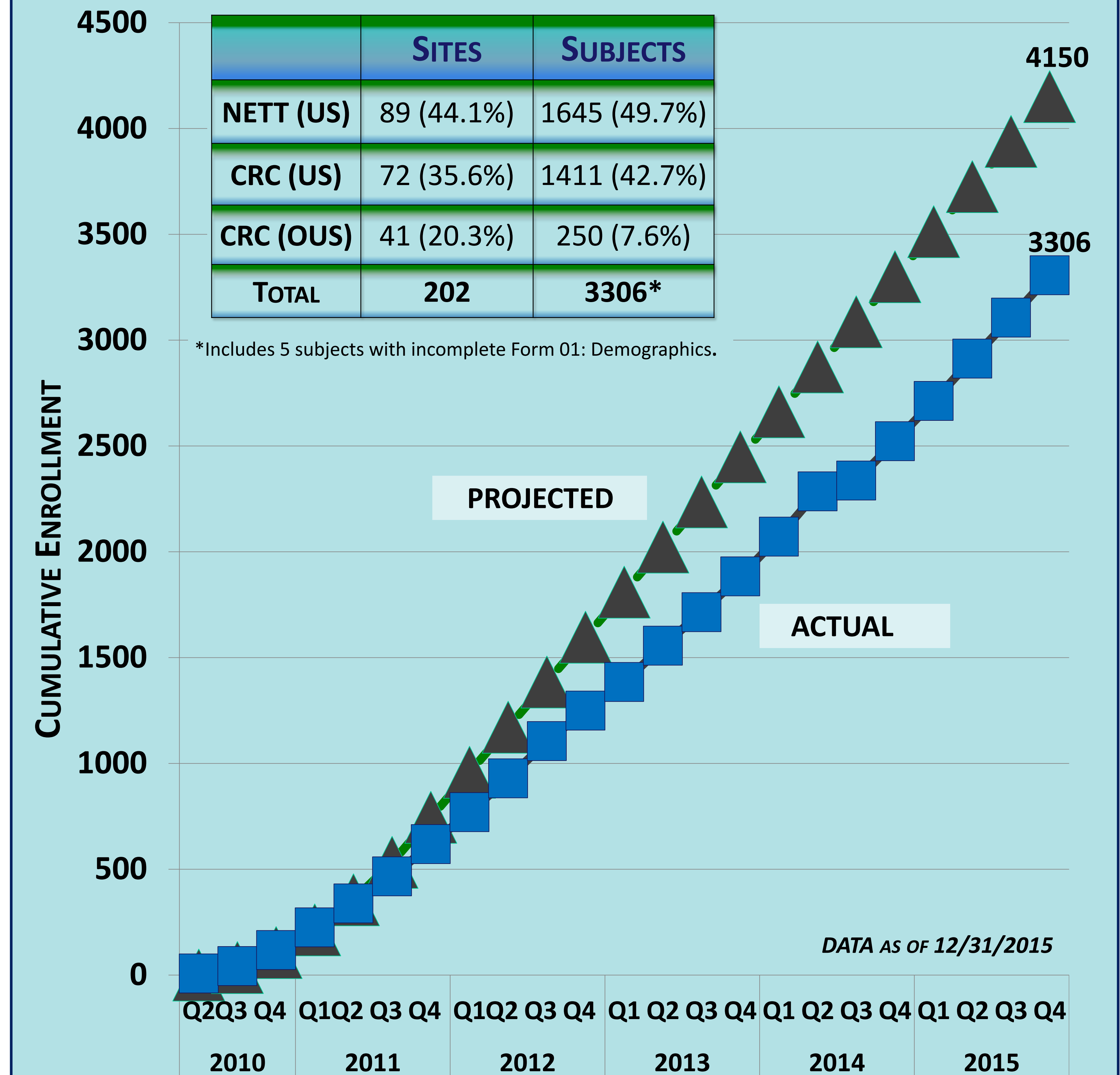
RANDOMIZATION

Subjects randomized 1:1 (clopidogrel: placebo), controlling for clinical center. Subject eligibility determined by site personnel prior to accessing the Randomization Module in WebDCU™, a web-enabled Clinical Trials Management System developed by the Neurological Emergencies Treatment Trials (NETT) Statistics and Data Management Center (SDMC) at Medical University of South Carolina (MUSC).

DEMOGRAPHICS AS OF 12/31/2015

GENDER	RACE	ETHNICITY
Male: 1751 (53.0%)	Asian: 89 (2.7%)	Hispanic or Latino: 235 (7.2%)
Female: 1550 (47.0%)	Black: 743 (22.5%)	Not Hispanic or Latino: 2934 (88.9%)
	White: 2360 (71.5%)	Not Reported/Unknown: 132 (3.9%)
	Other: 109 (3.3%)	

ACTUAL AND PROJECTED ENROLLMENT



TOP 6 ENROLLERS (AS OF 12/31/2015)

SPOKE (HUB)	#
Guilford Neurological Associates, Greensboro, NC (EMMES)	109
Hospital of the University of Pennsylvania, Philadelphia, PA (UPenn)	100
Benefis Hospitals Inc., Great Falls, MT (EMMES)	66
Stanford University Medical Center, Stanford, CA (Stanford)	60
Buffalo General Medical Center, Buffalo, NY (EMMES)	54
NYP Columbia University Medical Center, New York, NY (NYP)	54