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StrokeNet Prevention Working Group Update

October 7,2015 – Bethesda, MD

StrokeNet Prevention Working Group Membership


Thomas Brott


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StrokeNet Prevention Working Group Meeting through August 2015

01/15/15

02/19/15

04/16/15

05/21/15

06/18/15

07/16/15

08/20/15

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Top Priority Gaps in StrokeNet Prevention

(decided upon by the Working Group)

- **Optimizing medical management for secondary stroke prevention** including research on innovative systems to maximize delivery of care and strategies to bolster self-management skills, self- efficacy, medication adherence, and lifestyle change. Whether primary or secondary, prevention studies should be prioritized on the basis of knowledge gaps in evidence-based recommendations and modifiable targets.

- **Developing more effective early and long-term interventions for stroke subtype-specific secondary prevention** among high risk patients with intracranial atherosclerosis, cardioembolic stroke, small vessel disease (ischemic strokes and intracerebral hemorrhage), and cryptogenic infarcts including personalized pharmacogenetic approaches for antithrombotic medication selection.

- **Improving primary prevention** strategies including interventions for subclinical leukoarisosis progression/silent stroke, vascular cognitive impairment, asymptomatic aneurysms, and peri-operative stroke.

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Proposals Reviewed

Proposal by:

- **Natalia Rost, and Shyam Prabhakaran, *January 15th***
- **Randall Marshall, Ronald Lazar, David Liebeskind and E Sander Connolly, *February 19th***
- **Hooman Kamel and Elkind Mitchell, *April 16th***
- **Wade Smith, Randall Lee, and Karl Meisel, *May 21st***
- **Adnan Qureshi, *July 16th***
- **David Hasan, Robert Brown, and James Torner, *July 16th***
- **Maarten Lansberg, *August 20th***
- **Walter Kernan, et al *October 15th***

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Confidentiality

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Prevention studies underway

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Prevention studies in the peer review process

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Pre-Ischemic Conditioning for Intracranial AtheroSclerotic StrOke: PICASSO

Marc Chimowitz

David Hess

Hypothesis and Update

HYPOTHESIS: Subjects treated with Remote Limb Ischemic Conditioning plus Aggressive Medical Manangement in this trial will have a significantly lower rate of symptomatic cerebral infarction at 1 year compared with the rate observed in high-risk patients treated with AMM alone.

- Initial Grant Review (6/25/15): "tremendous excitement for the idea and the potential for significant impact....but a number of methodological issues raised"
- Study team are collecting more pilot data and completing re-design
- Plan to resubmit February 2016

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AtRial Cardiopathy and Antithrombotic Drugs In prevention After cryptogenic stroke (ARCADIA)

Hooman Kamel

Elkind Mitchell

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Hypothesis and Update

HYPOTHESIS: Apixaban is superior to aspirin for the prevention of recurrent stroke in patients with cryptogenic ischemic stroke and atrial cardiopathy.

- We submitted the application on June 2, 2015
- Scientific Review Group meeting will be held on November 11, 2015
- Recruitment start date, assuming funding, will be October 1st, 2016

We will be participating in two symposia scheduled for this coming year:

1) Beyond Atrial Fibrillation: Atrial Cardiopathies as a Cause of Unexplained Stroke – AHA International Stroke Conference.
2) Atrial Cardiopathies as a Cause of Cryptogenic Stroke: Beyond Atrial Fibrillation – European Stroke Conference.

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Carotid Revascularization and Medical Management for Asymptomatic Carotid stenosis - Hemodynamics (CREST-H)

Randolph Marshall

Ronald Lazar

David Liebeskind

E Sander Connolly

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Hypothesis and Design

HYPOTHESIS: Among CREST-2 patients who have impaired perfusion at baseline, there will be a difference in the change in cognitive performance between baseline and 1-year comparing**:**

1. **those assigned to CEA or CAS plus Intensive Medical Management**
2. **those assigned to Intensive Medical Management alone,** adjusting for age, baseline cognitive performance, depression, prior cerebral infarcts, subsequent silent infarction, WMH volume, and microbleeds.

- All CREST-2 patients get cognitive assessments at baseline, and yearly up to 4 years.
- Image 500 CREST-2 randomized patients using MRI gado-perfusion scan.
- 100 hemodynamically impaired (TTP delay >2 seconds); 400 hemodynamically normal
- Submitted to NINDS for October 3rd.

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Prevention studies almost ready for peer review

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Aneurysm Rupture Reduction and Expansion Stabilization Trial (ARREST)

David Hasan

Robert Brown

James Torner

Hypothesis and Update

HYPOTHESIS: Aspirin can attenuate the inflammatory process in cerebral aneurysm wall and decrease the incidence of aneurysmal growth and rupture

- Need to recruit more patients, 1716, because is we found both in humans and mice that there is gender differential response to aspirin. Males respond better than females.
- We need to enroll at 70 centers for recruitment.
- NINDS staff recommended that we do 3 years for recruitment and 4 years of maximum follow- up for a total of 7 years.
- NINDS staff will present our proposal to NINDS leadership in few days. If the budget is approved, we will aim to submit the grant application for the February cycle.

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Primary and Secondary prevention programs with MRI, white matter, and silent stroke

Natalia Rost

Shyam Prabhakaran

Clinton Wright

Rebecca Gottesman

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Hypothesis and Update

HYPOTHESIS: PRECISE MRI-T_2 is a trial of the safety and preliminary efficacy of aggressive blood pressure lowering (high-dose statin and target BP <120/80 mmHg) vs. standard of care in high-risk, stroke-free elderly individuals to prevent progression of silent cerebrovascular disease.

- Biweekly meetings since May with initial discussion of progression of white matter disease in ARIC and risk scores
- Reviewing SPRINT results and how they will impact the design of this proposed trial
- We are finalizing some key aspects about design, sample size, and power after which we should have the final concept form and initial budget numbers.

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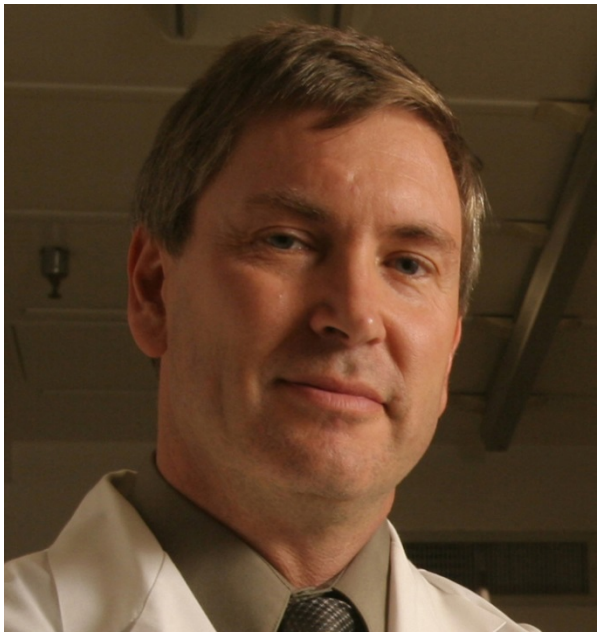
SOPRANO- StrOke PRevention in anticoagulant ineligible Atrial fibrillatioN by left atrial appendage Occlusion

Karl Meisel



Wade Smith

Randall Lee

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Hypothesis and Update

HYPOTHESIS: Our primary aim is to determine the safety and efficacy of left atrial appendage occlusion compared to medical therapy, to prevent the accumulation of additional FLAIR/T1 lesions of ≥ 3 mm on brain MRI at 2 years in high-risk patients with atrial fibrillation (A-Fib) who cannot tolerate oral anticoagulation.

- We have begun budget discussions with the CCC and the DMC (September 30th)

- Earliest possible date for submission will be February 2016.

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The PATCH TRIAL: Detection of Paroxysmal Atrial Fibrillation after Small or Large Vessel Ischemic Stroke

Maarten Lansberg

Mintu Turakhia

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Hypothesis and Update

HYPOTHESIS: Determine whether the yield of atrial fibrillation detection is higher in the cardiac patch monitoring group than in the standard of care group at 28 days.

- Patients will be eligible if they are within 1 month of an ischemic stroke secondary to small or large vessel disease, have no history of atrial fibrillation, and no evidence of atrial fibrillation on routine cardiac work-up.
- Patients will be randomized (1:1) to a cardiac patch group who will undergo 28 days of cardiac patch monitoring or a standard of care group who will receive medical follow-up without additional cardiac monitoring.
- We need to enroll at 25 stroke centers for recruitment.
- Need to enroll 1200 stroke patients.
- The pragmatic trial design is ideally suited for the StrokeNet infrastructure.

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Extracranial Vertebral Artery Stenosis Treatment Trial

Adnan Qureshi

Michael Parides

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Hypothesis and Update

HYPOTHESIS: Endovascular treatment plus intensive medical therapy of moderate to severe vertebral artery origin stenosis reduces the risk (hazard) of recurrent vertebrobasilar arterial distribution ischemic stroke in patients with vertebrobasilar arterial distribution ischemic events, transient ischemic attack or minor ischemic stroke.

- Need to recruit 1270 patients. The proposed trial is event driven, with 283 primary endpoint events required to achieve the desired power of 90%. Total of 300 patients recruited so far.
- Patient follow-up is expected to continue for 12 months following randomization of the last patient. Assuming uniform accrual over a 36 month period, patients would be followed for a range of 12-48 months, with median follow-up of 30 months.
- Total of 140 sites.

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Prevention studies on the calendar

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THANKS FOR YOUR ATTENTION