NIH StrokeNet
PREVENTION | TREATMENT | RECOVERY

NIH StrokeNet Meeting

3-June, 2014 10:00 am – 4:00 pm

Crystal Gateway Marriott

MUSC
MEDICAL UNIVERSITY of SOUTH CAROLINA

NIH
Funded by a grant from the National Institutes of Health

UNIVERSITY OF Cincinnati

Welcome

- *Brief* Agenda Overview
  - Specific Ongoing Trials/Studies
    - MISTE III
    - CREST 2
    - I DEF
    - PCORI
    - Existing SPOTRIAS Trials
  - Working Lunch with Q and A
  - Educational Core Update
  - StrokeNet WebDCU Orientation
  - Breakouts for Educational Core, and Working Group discussions

National Data Management Center

- Yuko Palesch
- Wenle Zhao
- Catherine Dillon
- Jessica Simons
- Jordan Elm
- Renee Martin
- Sharon Yeatts
- Jaemyung Kim

FOA Updates –Dr. Janis

- **May 14, 2014:** U01 Funding Announcement for the network published.PAR-14-220: NIH StrokeNet Clinical Trials and Biomarker Studies for Stroke Treatment, Recovery, and Prevention (U01)

- X01 (the company companion mechanism) - (pending)

- SBIR (Small Business) - (pending)

Specific Ongoing Trials/Studies Presentations and Q and A

Ongoing SPOTRIAS Trials

- STOP-IT
- CLEAR-FDR
- DESERVE
- ARTSS-2
- MR-WITNESS
- NeuStart Phase 2
- ICTUS 2

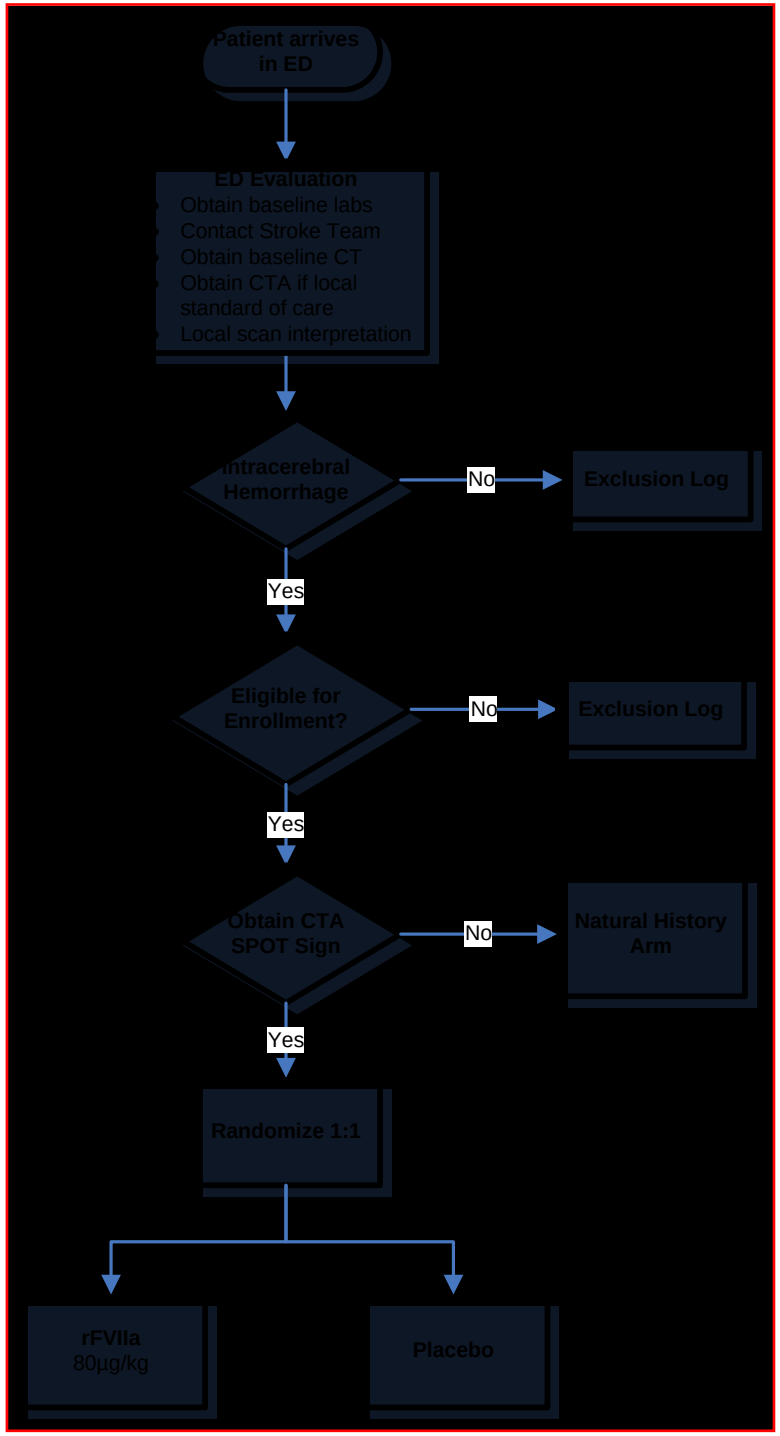
STOP-IT: Study Hypotheses

- Confirm in a prospective study:
  - Sensitivity and specificity of CTA spot sign for hematoma growth
- Determine:
  - Feasibility of CTA to identify ICH patients at high risk of hematoma growth and select patients for randomization to treatment with rFVIIa or placebo
- Randomize ICH patients presenting within five hours of onset with a spot sign to treatment with rFVIIa, at 80 µg/kg vs placebo to:
  - Determine if rFVIIa is effective at reducing hematoma growth among patients with a spot sign
  - Provide preliminary efficacy data for treatment paradigm

STOP-IT Study Design

- Treatment criteria*
  - Age 18-80 years
  - Baseline CT within 5 hours from onset
  - ICH volume 0.5 - 90 cc
  - GCS > 8 at presentation
  - Pre-admission mRS score < 2
  - No prior thromboembolic history
  - Baseline troponin WNL
  - For spot positive patients, dosing of study drug within 90 minutes of enrolling CT scan
- Not looking for additional sites (limited medication supply)
- Matt Flaherty, PI

***Partial list**



CLEAR-FDR : Combined Approach to Lysis Utilizing Eptifibatide and rt-PA in Acute Ischemic Stroke-Full Dose Regimen

- Primary objective - estimate sICH rate in AIS patients treated with rt-PA (0.9mg/kg) within 3 hours of symptom onset plus eptifibatide (bolus 135 mcg/kg and 2 hour infusion at 0.75 mcg/kg/min)

- Design – single arm, prospective open label study

CLEAR-FDR

- Stopping Rules – Enroll up to 30 patients; stop if 3 sICH cases within the first 19 patients or 4 sICH cases within 29 patients (i.e., sICH rate ~>8%)
- Inclusion – age 18-85, NIHSS ≥6
- 12 of 30 cases enrolled to date
- Not currently planning on recruiting additional sites
- Dr. Adeoye PI

DESERVE Trial : Discharge Educational Strategies for Reduction of Vascular Events

Specific Aims

To evaluate the effectiveness of an innovative multi-level discharge intervention (skills, chronic care model, bilingual research health workers) versus standard discharge care on vascular risk reduction (BP, smoking, HbA1C, etc) among mild stroke/TIA patients at 12 months post discharge.

Secondary Aims

1. Comparison of secondary stroke events

2. Analyze the independent contributions of Risk Perception, Adherence, Patient Physician Communication to primary outcomes.

PI Bernadette Boden-Albala
P50 NS049060 (P2)

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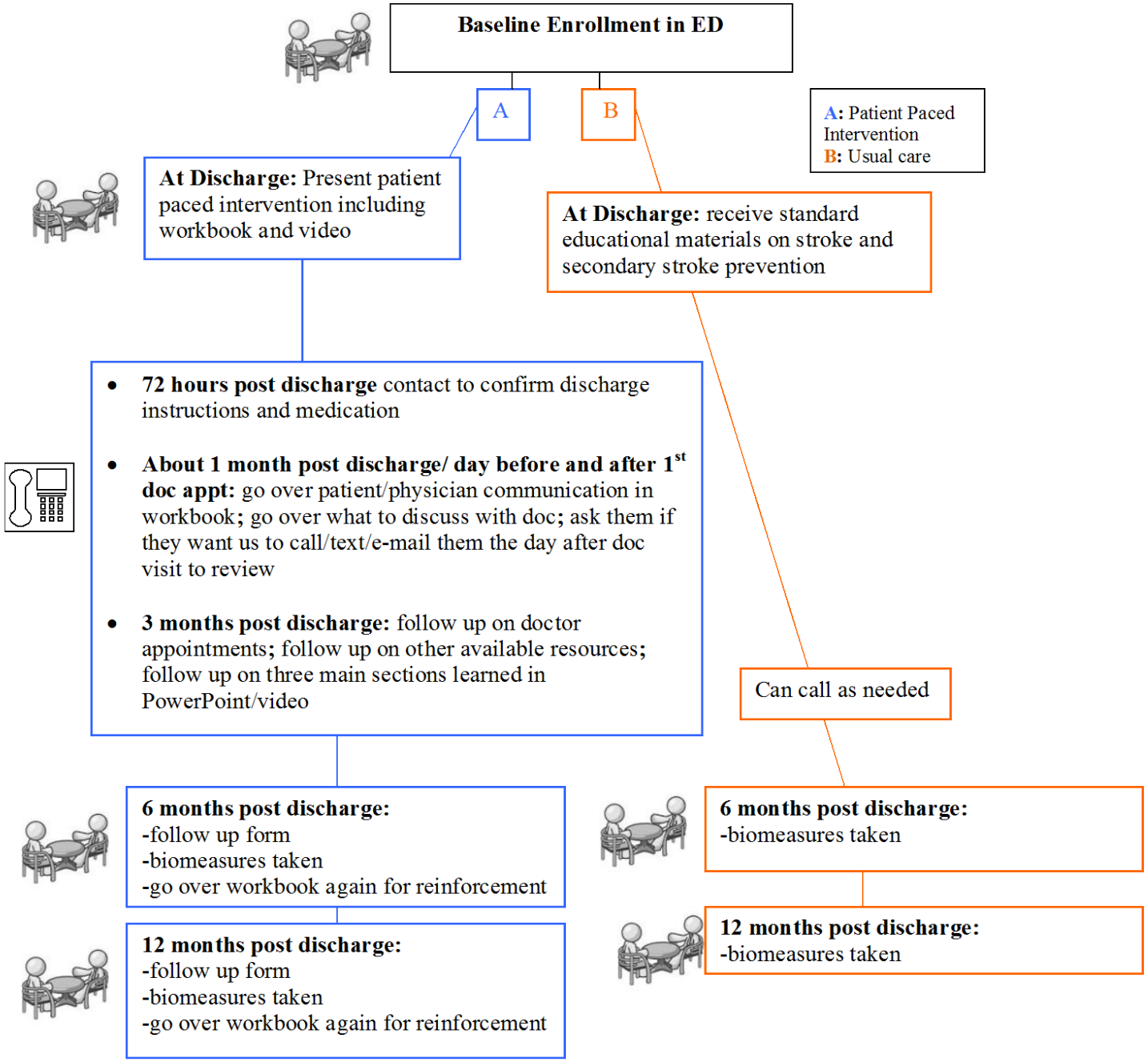


DESERVE is an innovative patient-paced, multi-level behavioral discharge intervention aimed at secondary stroke prevention through risk factor reduction in 800 mild stroke/TIA patients.

307 patients enrolled from NYU, Mount Sinai and Columbia.

Inclusion Criteria

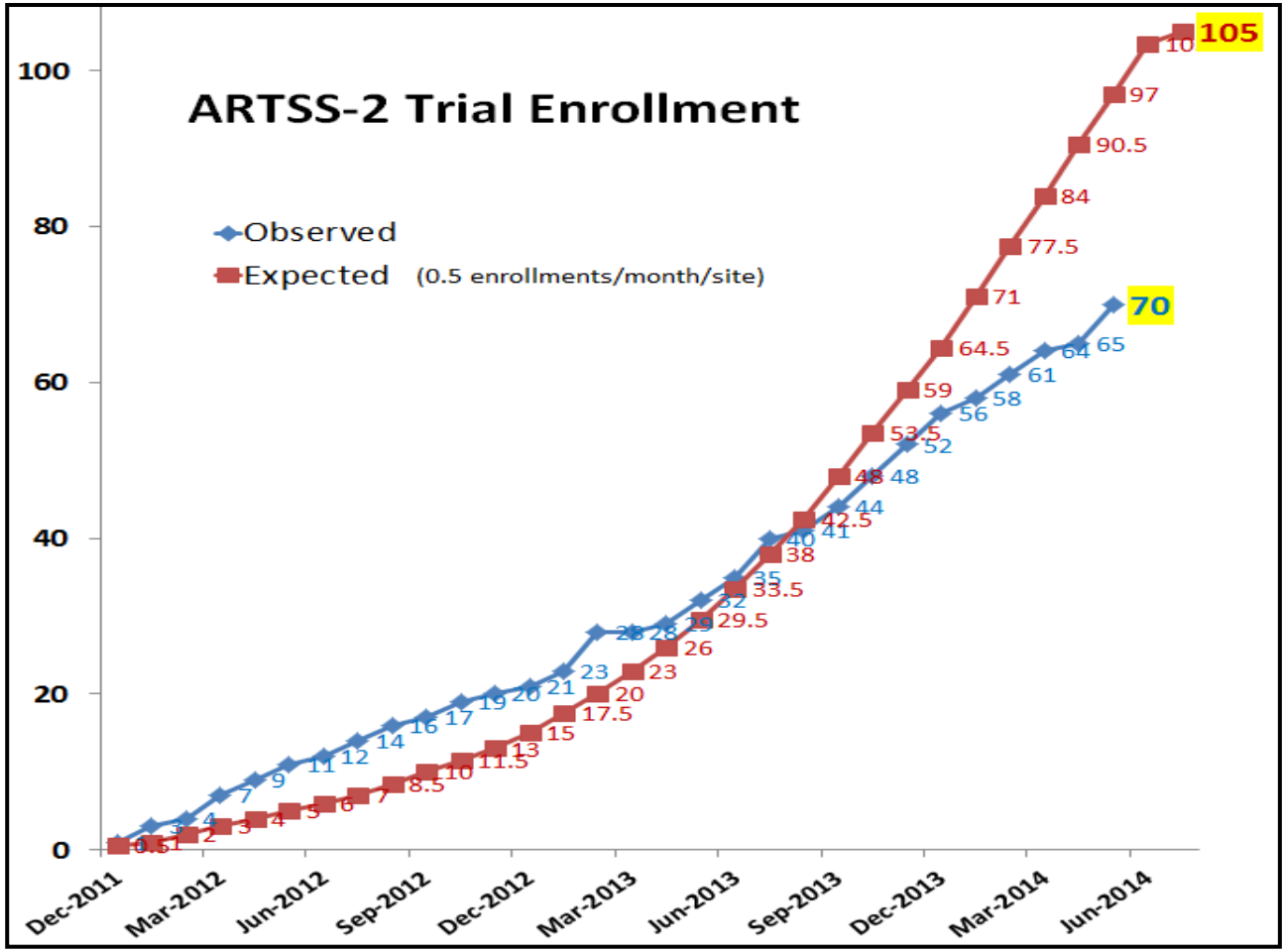
- Mild Stroke & TIA patients (consentable without waiver)
- NIHSS $\leq$ 5
- Vascular Risk Factors; including: Hypertension; Smoking ; Metabolic Syndrome

Exclusion Criteria

- Unable to consent
- Resides or discharged to skilled nursing facility
- Poor survival odds over the study course (12 months)

ARTSS-2: Phase IIb, randomized, multi-center trial of Argatroban in combination with recombinant tissue plasminogen activator for acute stroke

- *Andrew Barreto*, MD MS, Co-PI
- *James Grotta*, MD, Co-PI
- *Gary Ford*, MD, UK Chief Investigator
- *Mohammad H. Rahbar*, PhD, PI – Data Coordinating Center
- Argatroban – Direct Thrombin Inhibitor
- ARTSS-1 *Stroke* 2012, 43:770-775
  - 0.9mg/kg tPA + low-dose Argatroban × 48 hours
  - Three sICH (4.6%); Total study n=65
  - 40% complete recanalization of proximal intracranial occlusions at 2-hours (13% historical controls with t-PA-alone)



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ARTSS-2

- **Major inclusion criteria**
  - **0-4.5 hour tPA**-treated patients (following ECASS-3 exclusions)
  - **Age ≥ 18** (no upper limit)
  - **NIHSS ≥10**
    - Or any NIHSS if clot demonstrated in proximal intracranial artery
  - **INR ≤ 1.5**
  - PTT within lab normal range
  - **mRS <2**
  - No endovascular therapy

- **Randomized to 1of 3 treatment arms (n=35 each):**

1) **Low-dose** Argatroban will receive:
   - 100 μg/kg bolus then continuous infusion of 1.0 μg/kg/min for 48 hrs.
     Target aPTT of **1.75 x baseline**

2) **High-dose** Argatroban will receive:
   - 100 μg/kg bolus then continuous infusion of 3.0 μg/kg/min for 48 hrs.
     Target aPTT of **2.25 x baseline**

3) **Intravenous-rt-PA alone**

- **Behind Recruitment**
  - Many sites are underperforming
  - At current rate, study will complete in 1st-2nd Quarter 2015
  - We are very open to [a small handful] of motivated centers who would like to join the study

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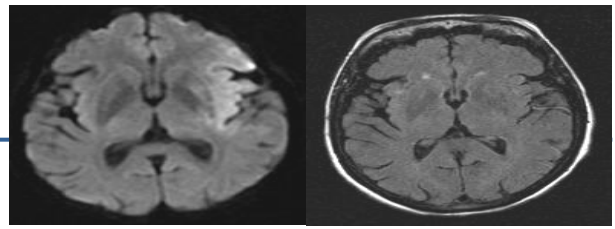
MR WITNESS



Inclusion/Exclusion Summary

- 80 adult subjects age 18-85 with acute ischemic stroke
- Treatment with IV tPA between **4.5 h to 24 h since Last Known Well (LKW), and within 3 hr of symptom discovery**
- Ineligible for on-label rt-PA
- Clinically disabling symptoms and an NIH Stroke Scale score of <=25
- Otherwise eligible to receive rt-PA using usual clinical criteria (except time)
- No contraindications to MRI
- Admission MRI:
  - DWI Positive but FLAIR-negative or faintly positive (defined as a mean signal intensity ratio of 1.15 compared to FLAIR lesion less than 15% of normal tissue.
  - No evidence of CAA

Safety Outcomes

- **Primary Outcome**: No significant increase in symptomatic intracranial hemorrhage rates c/w ECASS 3 (rate 5.3%; 95%CI: 3.3-7.9%) with predefined stopping rules
- **Secondary Outcome**: No significant increase in symptomatic brain edema with mass effect as the predominant cause of clinical deterioration c/w ECASS3 (rate 6.9%; 95%CI: 4.6–10.1%)

MR WITNESS: Study Progress

- 43/80 (54%) subjects enrolled at 5 sites
  - MGH, NINDS, UT Seton, WUSTL, UCLA, Cedar-Sinai
  - Seeking to add 5-10 additional sites (5 of these contracts pending)
- DSMB has met 3 times and there are no safety concerns
- Interested sites should contact Lee Schwamm (lschwamm@mgh.harvard.edu)
- clinicaltrials.gov/NCT01282242

NeuSTART - Phase 2

- PI: Mitch Elkind, Columbia University
- NIH/NINDS P50 NS049060 (Marshall)
- Contact: mse13@columbia.edu
- **Hypothesis**: Short-term ultra-high-dose statin therapy is feasible and safe in patients with acute ischemic stroke.
- **Primary Aim:** Determine whether lovastatin 640 mg daily for 3 days beginning within 24 hours after acute stroke can be administered **safely**.
- **Secondary Aim:** Assess **efficacy** of lovastatin administered at high doses.

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NeuSTART 2: Key Points

Key Inclusion criteria:

- ISCHEMIC STROKE WITHIN 24 hrs
- AGE ≥18
- NIHSS ≥2
- IV/IA rt-PA allowed
- No history of significant liver or muscle disease

Primary outcome: Liver or muscle complications

Secondary outcomes: Barthel and mRS at 90 days

Sites: Columbia, BWH-Partners (Feske), Univ Miami (Romano), Mount Sinai (Dhamoon), UCLA (Starkman)

Progress to date: 80 patients enrolled; looking for 80 more

Advantages: 1. Includes patients who would may not be eligible for other acute trials.

WE ARE LOOKING FOR ADDITIONAL SITES! Contact: Mitch Elkind: mse13@columbia.edu

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ICTuS 2

- **Investigational intervention:**
- Endovascular hypothermia to 33°C, followed by rewarming over 12 hours to 36.5°C Group 1, best medical therapy with normothermia (Group 2). - randomization: 1:1
- **Study Population:**
- Acute Ischemic Stroke, treated with IV tPA < 3hours, age 22-82, NIHSS 7-20 (left), 7-24 (right hemisphere)
- **Primary aims of the trial:**
- To determine whether the combination of intravenous thrombolysis and hypothermia is superior to thrombolysis and normothermia for the treatment of acute ischemic stroke.
- **Status of ICTuS 2 (SPOTRIAS)**
- On target to meet SPOTRIAS milestones (safety, feasibility of protocol, feasibility of hypothermia).
- **Role of StrokeNET:**
- The study will be a Phase 3 pivotal efficacy study that follows a SPOTRIAS funded Phase 2 safety and feasibility trial using the identical protocol. Now that safety and feasibility are established, recruitment though StrokeNet will provide the essential boost to meet final recruitment target.

•Enrolling sites

- Alexian Brothers, IL
- Abington Memorial, PA
- CHUV, Lausanne Switzerland
- Colorado Neurological, CO
- Columbia University, NY*
- Cedars Sinai, CA*
- University of Colorado, CO
- Hartford Hospital, CT
- UCSD, CA*
- Scripps Mercy Hospital, CA*
- Michigan State Univ, MI
- North Memorial, MN
- Sarasota Memorial, FL
- University of Florida, FL
- University of Miami, FL*
- UT Houston, TX*
- Yale University, CT

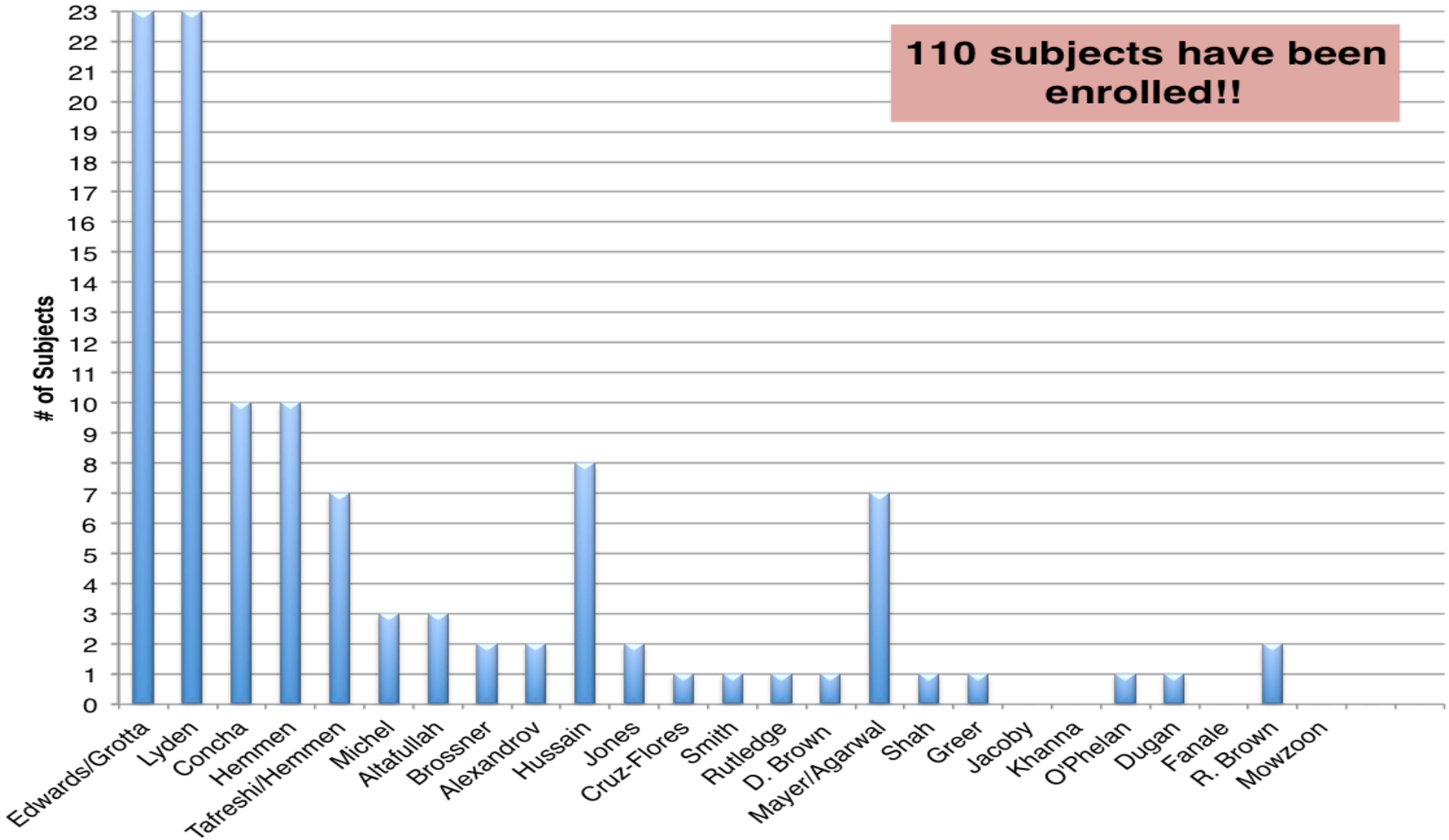
*StrokeNET site

Additional sites in start-up

- Lee Memorial-Gulf Coast, FL
- UT Southwestern, Dallas-TX
- University of Toledo, OH
- Henry Ford, MI*
- University of Louisville, KY
- Intermountain System, UT
- Baylor University, Dallas-TX
- Lehigh Valley Hospital, PA
- Ochsner Clinic, New Orleans-LA
- Medical College of Wisconsin*

Pat Lyden, P.I.

Total Enrollment by Site (as of 05/27/14)



NCC Staff Change and Opportunity

- Laura Sauerbeck is retiring for family reasons.
- Judy Spilker will be assuming Laura's role but Judy's position is now open. Opening of position both internally and externally.
- The new posting for the pending vacancy within the NCC StrokeNet team is entitled **CLINICAL RESEARCH ADMINISTRATOR/DIRECTOR**.
- If interested in applying, please visit www.jobsatuc.com
  - Upper left hand side of the screen, you'll see SEARCH POSTINGS. Click there.
  - Type 214CM8310 in the field Position Number
  - Click SEARCH.
- Also can contact Rose Beckman for further information.