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The Newsletter of the POINT Trial

Volume 1, Issue 5 4th Quarter 2011

Looking Back on 2011 and Ahead to 2012

Dear Colleagues,

On December 31, 2011, we enrolled our 619th subject, at Guilford Neurologic in Greensboro, NC, putting us close to 15% of our overall goal of 4150 subjects for the POINT Trial.

Looking Back: 2011

At the end of fourth quarter of 2011, there are 139 activated sites ready to enroll in POINT, just over 90% of our target of 150 US sites. 114 of those sites have at least 1 enrollment, for a total of 619 subjects as of the end of December. December was a record month despite the holiday break, with 54 enrollments for the month alone!

While we did fall short of our target enrollment of 745 subjects by the end of 2011, with more sites coming online and renewed focus and energy in the new year, we're confident we can make up the shortfall and reach if not exceed our 2012 goal of 1596 subjects.

Looking Ahead: 2012

ARRA Funding Conversion to U01 Grant
With the stimulus funding from the American Recovery and Reinvestment Act (ARRA) of 2009 coming to a close, we'll be transitioning the source of POINT funding to a U01 Grant. ARRA funding is restricted to domestic sites only, so the new U01 Grant will allow us to increase enrollment with an international base of subjects.

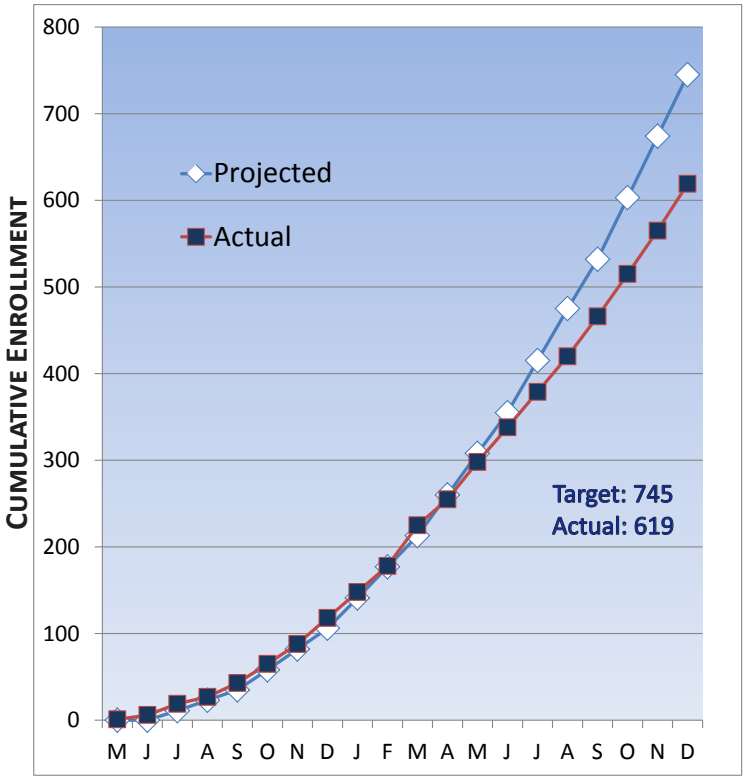
International Expansion
We're looking forward to getting our new sites up and running next year! Australia, Canada, Chile, Ecuador, Israel, Mexico, New Zealand, Peru, Spain, Taiwan, and the United Kingdom all have sites lined up to join POINT and help recruit enrollments. Our overall target of 210 actively enrolling sites includes a goal of 60 international sites.

Please don't hesitate to contact us directly if you have questions or would like more information. We're looking forward to a great new year for POINT, and appreciate all your hard work.

Sincerely,
Clay Johnston MD, PhD, POINT Trial Principal Investigator
Don Easton MD, POINT Trial co-Principal Investigator

In This Issue

POINT Cumulative Enrollment
May 2010 through December 2011



POINT Enrollment Update: Total=619

***Top Enrollers** (as of December 31, 2011)*

Site (Hub)	City	State	#
Guilford Neurologic (CRC)	Greensboro	NC	50
Hospital of UPenn (UPenn)	Philadelphia	PA	29
Detroit Receiving (Wayne)	Detroit	MI	21
University of Kentucky (Kentucky)	Lexington	KY	18
Henry Ford (HFHS)	Detroit	MI	18
OHSU - Oregon (OHSU)	Portland	OR	16
Colorado Neuro Institute (CRC)	Englewood	CO	15
Advanced Neurology Specia (CRC)	Great Falls	MT	14
Beaumont Royal Oak (Wayne)	Royal Oak	MI	13
Mayo Arizona (CRC)	Phoenix	AZ	12
Froedtert Mem Hosp (Wisconsin)	Milwaukee	WI	12
Abington (UPenn)	Abington	PA	11
Memorial Hermann (Texas)	Houston	TX	11
Northwestern University (CRC)	Chicago	IL	10
NYP - Columbia	New York	NY	10
Palmetto Health Richland (CRC)	Columbia	SC	10
Bon Secour (CRC)	Midlothian	VA	10
Temple Univ Hospital (Temple)	Philadelphia	PA	10
Hennepin County Med Ctr (MN)	Minneapolis	MN	10
Emory Univ Hosp (Emory)	Atlanta	GA	10

Sites with 6-9 subjects enrolled:	17
Sites with 1-5 subjects enrolled:	77
Sites with 0 subjects enrolled:	25

Send your feedback and suggestions for future newsletters to Mary.Farrant@ucsfmedctr.org

Premature Cessation of Study Drug, Consent Withdrawal, and Lost to Follow-up

The number of subjects who prematurely stop study medication permanently, withdraw consent, or are lost to follow-up and their vital status is unknown at the end of the study, are all important in assessing the integrity, rigor and interpretation of the results of clinical trials.

There are legitimate reasons for premature cessation of study drug, such as the need for guideline-recommended anticoagulation (e.g., development of atrial fibrillation) or clopidogrel (e.g., coronary stent placement), but efforts should be made to minimize them. Discontinuing study drug after a primary outcome occurs to switch to another antithrombotic should be discouraged. If we knew whether another drug was better than the study drug, even after an outcome event, we would not be conducting POINT. In addition, there is more than the primary objective to POINT. We also want to know if a subject dies from a huge stroke a month after experiencing a minor stroke (i.e., after a primary outcome) on study drug, and the effectiveness of 90 days of dual antiplatelet therapy. We won't answer these questions if patients come off study drug.

If subjects discontinue study drug prematurely, we still want them to complete all follow-up visits, particularly their 90-day follow-up. The primary analysis in POINT is by intention to treat, so all outcomes in the 90-day period count whether or not the subject is on study drug. For subjects who are lost to follow-up, sites need to complete the CRFs for the subject's last follow-up visit, whether 7-day or 90-day. If a patient cannot make the 90-day follow-up visit, please collect as much information as possible about vital status and whether an outcome occurred during their 90 days in the trial, even if this is just through a phone contact.

October-December Completed Readiness Calls *(listed alphabetically)*

Site (Hub)	City	State
Christiana (UPenn) ‡	Newark	DE
Cleveland Clinic (CRC) ‡	Cleveland	OH
Dartmouth Hitchcock (CRC) ‡	Lebanon	NH
Innovative Medical Research (CRC)	Aventura	FL
Kings County Hospital (CRC) ‡	Brooklyn	NY
Maimonides Medical Center (CRC)	Brooklyn	NY
Mercy Hospital Buffalo (CRC) ‡	Buffalo	NY
O'Connor Hospital (Stanford)	San Jose	CA
St. Joseph Mercy Hospital (HFHS)	Ann Arbor	MI
St. Joseph Regional Health Ctr (Texas)	Bryan	TX
Sutter Roseville (CRC) ‡	Roseville	CA
UCSD Thornton Hospital (CRC)	La Jolla	CA
West Virginia University (CRC)	Morgantown	WV

‡ Has 1 or more enrollment

COORDINATOR'S CORNER

by Aaron Perlmutter, POINT Program Coordinator at MUSC, and Tess Bonham, CCRP, POINT Site Manager at the NETT

Preventing Study Drug Crossover

In POINT, subjects are randomly assigned to one of two treatment arms: clopidogrel plus aspirin, or placebo plus aspirin. The primary analysis in POINT is intention to treat, or ***ITT***, and includes all randomized subjects. The basic principle of ITT is that the effect of a treatment intervention can be best evaluated by the intention to treat a subject (i.e., placebo or clopidogrel, to which they were randomized, regardless of whether they received or adhered to their allocated intervention.

One way to ensure that subjects can be correctly analyzed in the groups to which they were randomized is to minimize ***crossover***. Crossover occurs in POINT when a subject is accidentally put into the opposite arm of the study to which he or she was randomized by being given a bottle of study drug different from the one assigned. This can dilute the treatment effect between the two arms of the study and have a significant impact on final outcomes.

To reduce randomization crossovers, changes will be made to **Form 10: Randomization** to include a link to a ***Randomization Verification Form.*** When clicked, the link opens a form that site personnel will print, take to the investigational pharmacy (or other study drug location) and complete when study drug is dispensed. This additional step should reduce the chances of crossover by requiring site personnel to compare the Study Drug ID assigned automatically by WebDCU™ and pre-printed on the form, to the Study Drug ID on the bottle of study drug that is dispensed by the pharmacy. Verification that the two Study Drug ID numbers match **must** take place before the loading dose is given to the subject.

The Randomization Verification Form will contain the following information:

- **Subject ID __ __ __ __** (The 4-digit **Subject ID** will be pre-printed on the form by WebDCU™.)
- **Study Drug ID assigned by WebDCU™ __ __ __ __** (The 4-digit **Study Drug ID** will be pre-printed on the form by WebDCU™.)
- **Study Drug ID on bottle retrieved from the pharmacy/other study drug storage location: __ __ __ __** (The person completing this form will enter the 4-digit **Study Drug ID** from the bottle on the form.)
- **Signature of the person verifying WebDCU™ Study Drug ID matches the Study Drug ID on the bottle retrieved from the pharmacy/other study drug storage location. _____** (The person completing this form will sign and print his or her name after making sure the two Study Drug ID numbers match.)

NOTE: The Randomization Verification Form should be filed with the other source documents for the subject.

When to Complete an Outcome Event Visit

An Outcome Event Visit should only be conducted if a subject experiences an ischemic stroke, TIA, or myocardial infarction. Outcome Event Visits for myocardial infarction can be done via telephone. All other Outcome Event Visits must be conducted in person. For all other SAEs/outcome events, simply submit Form 19: SAE/Clinical Outcome Reporting Form.

Questions? Contact Aaron Perlmutter, at ***perlmutt@musc.edu*** or (843) 876-1261.