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The Newsletter of the POINT Trial

Volume 2, Issue 2 2nd Quarter 2012

2012 2nd Quarter Recap

Minimizing Subjects Lost to Follow-Up

Dear Colleagues,

With 159 sites activated, and 137 with at least 1 enrollment, our target for US sites has been met. As of June 30, there are 929 subjects enrolled, bringing us to 22.4% of our overall goal of 4150 subjects enrolled in POINT.

International expansion is expected to begin in January of 2013, and the POINT-CRC, which will be responsible for activating and managing sites outside the US, has been working hard to meet that deadline.

Subjects Lost to Follow-Up

The growing number of subjects lost to follow-up (LTFU) in POINT is a concern; see the chart to the right. The recent amendment to the protocol scheduled for release on July 20, 2012, in addition to other amended study documents, contains a few changes to the way in which subjects are considered to be lost to follow-up.

A subject is considered lost to follow-up when continued contact with the subject cannot be maintained AND, despite an active follow-up effort, the site is unable to collect reliable information about the outcome event status of the subject during their 90-day enrollment period. The information from their 90-day enrollment period may be collected up to 150 days following randomization.

This expanded window of 150 days from randomization gives sites additional time to attempt to reach the subject, and should help minimize the number of subjects described as LTFU.

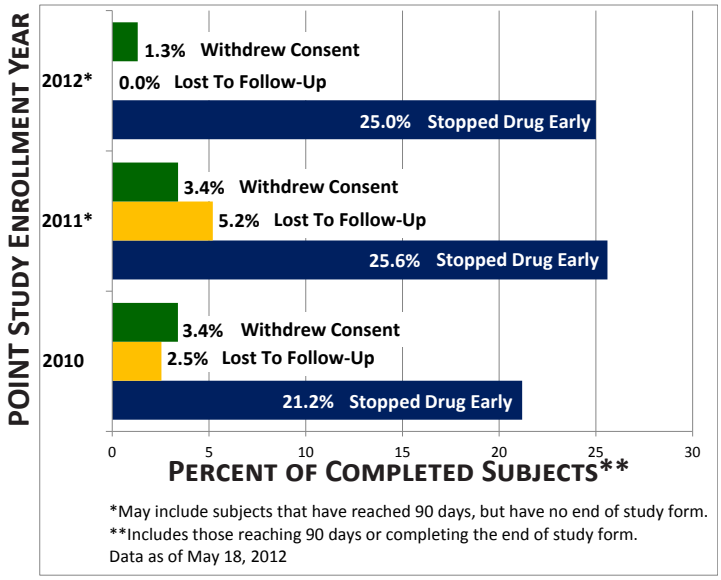
90-Day Telephone Follow-up Added

While the 90-day follow-up should be completed during an in-person visit whenever possible, under limited circumstances, for example, if the subject is unable to come in for follow-up due to illness, the visit may be completed by telephone. CRF completion for the visit will be guided by whether the visit was conducted by phone or in person, and a script for use in completing the telephone follow up will be available soon.

Please don't hesitate to contact us directly if you have questions or require more information.

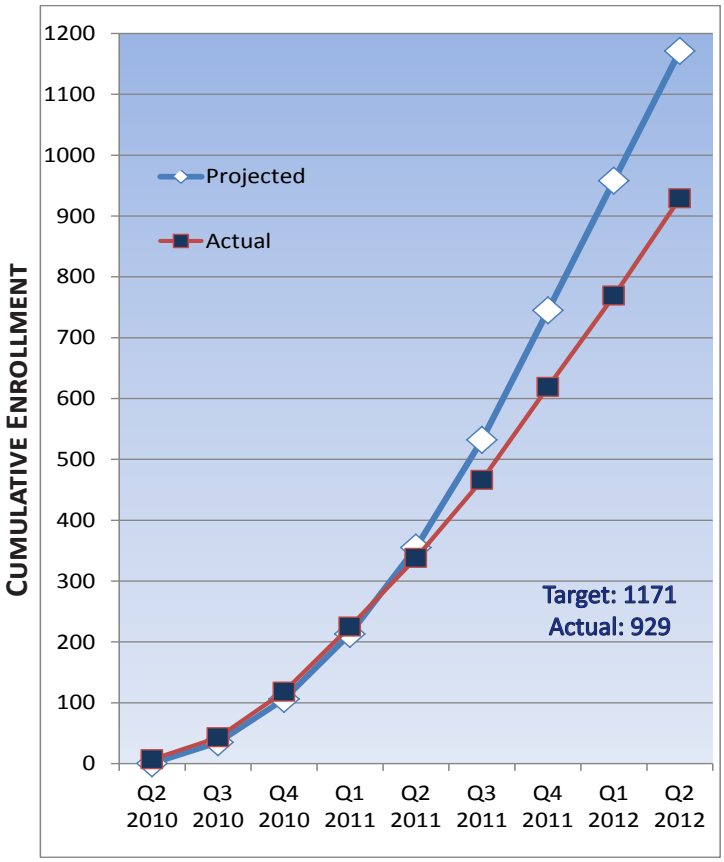
Sincerely,
Clay Johnston MD, PhD, POINT Trial Principal Investigator
Don Easton MD, POINT Trial co-Principal Investigator

Withdrawn Consents, Losses to Follow-Up, and Stopped Drug Early



*May include subjects that have reached 90 days, but have no end of study form.
**Includes those reaching 90 days or completing the end of study form.
Data as of May 18, 2012

POINT Cumulative Enrollment
May 2010 through June 2012



POINT Enrollment Update: Total=929

In This Issue

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

POINT Frequently Asked Questions (FAQs)

Q. Although use of tPA is an exclusion for entry into POINT, if a patient is already enrolled and treated with the loading dose of clopidogrel/placebo plus aspirin, and then develops a new or worsening stroke, can s/he be treated with tPA?

A. Yes. The SITS (Safe Implementation of Treatments in Stroke) investigators created a 15-point Symptomatic ICH (SICH) score, the SITS SICH risk score, for predicting ICH after giving tPA (see Table 2 in Stroke. 2012;43:1524-1531). Aspirin added 2 points of 15 to the risk of SICH and about half of patients in POINT will already be on aspirin before enrollment, and more will receive it in the Emergency Department. Use of clopidogrel added 1 additional point. The investigators concluded, "We cannot propose withholding treatment with alteplase in patients otherwise eligible according to current guidelines." Also see Arch Neurol. 2008;65:607-611 and 575-576.

In the Third International Stroke Trial (Lancet 2012; published online May 23), 51% of the tPA-treated subjects were treated with 'antiplatelet drugs' in the previous 48 hours, it was 40% in the NINDS rt-PA Stroke Study, and there was a slight trend toward a greater benefit in this group for the primary endpoint: the proportion of patients alive and independent at 6 months.

Given this information, POINT recommends that patients who meet all POINT criteria for enrollment be enrolled and administered study drug and aspirin promptly. If they subsequently develop a new or worsening stroke and meet guidelines for tPA treatment, they should be given tPA. Although this will be considered a protocol violation, we recognize that optimal individual patient management may dictate deviating from the protocol from time to time. Patients and families should be told that pre-existing use of antiplatelet therapy might slightly increase the risk of symptomatic ICH.

April-June Completed Readiness Calls *(listed alphabetically)*

Site (Hub)	City	State
Duke University Medical Center (CRC)	Durham	NC
Hackensack University Medical Center (Temple)	Hackensack	NJ
Michigan State University (CRC)	East Lansing	MI
Rush University Hospital (Wisconsin)	Chicago	IL
The Brain and Spine Research Institute (CRC)‡	Los Angeles	CA
Tucson Medical Center (Arizona)	Tucson	AZ
University of Florida Gainesville- Shands (CRC)	Gainesville	FL
University of New Mexico (Arizona)‡	Albuquerque	NM
University of Washington Medical Center (CRC)‡	Seattle	WA
William Beaumont Hospital- Troy (Wayne)	Troy	MI

‡ Has 1 or more enrollment

Top Enrollers *(as of June 30, 2012)*

Site (Hub)	City	State	#
Guilford Neurologic (CRC)	Greensboro	NC	62
Hospital of UPenn (UPenn)	Philadelphia	PA	35
Detroit Receiving (Wayne)	Detroit	MI	25
Henry Ford (HFHS)	Detroit	MI	24
University of Kentucky (Kentucky)	Lexington	KY	21
Advanced Neurology Specialists (CRC)	Great Falls	MT	19
Beaumont Royal Oak (Wayne)	Royal Oak	MI	19
Memorial Hermann (UT Houston)	Houston	TX	18
Colorado Neuro Institute (CRC)	Englewood	CO	18
Mayo Arizona (CRC)	Phoenix	AZ	17
OHSU - Oregon (OHSU)	Portland	OR	17
Abington (UPenn)	Abington	PA	16
Mission Hospital (CRC)	Asheville	NC	16
Kaleida (CRC)	Buffalo	NY	16

Sites with 11-15 subjects enrolled:	13
Sites with 6-10 subjects enrolled:	28
Sites with 1-5 subjects enrolled:	82
Sites with 0 subjects enrolled:	22

COORDINATOR'S CORNER

The POINT Biomarkers Ancillary Study

by Trese Biagini, RN, MA, POINT Clinical Research Nurse

Starting in August of this year, enrollment will begin for the POINT Biomarkers Ancillary study, involving a single blood draw at time of enrollment.

What exactly is a biomarker? A biomarker has been defined in the recently revised consent for POINT as a distinct molecule found in blood, other body fluids, or tissues that is sign of a specific condition or disease.

What is the POINT Biomarkers Ancillary Study? Back in 2012, the FDA issued a warning about ***clopidogrel resistance***: reduced effectiveness of clopidogrel in patients who are "poor metabolizers" of the drug. At that time, the FDA informed healthcare professionals about tests available to identify genetic differences in these poor responders, especially in CYP2C19 function.

The **POINT Biomarkers Ancillary Study** will include testing the blood of consented POINT participants to determine inherited clopidogrel resistance. This would be the first systematic study of clopidogrel resistance in the setting of stroke prevention following TIA and minor ischemic stroke. Per subject reimbursement will vary by the type of analysis and specimen processing requirements. Sites may participate in collecting *DNA only* with a $150 per subject reimbursement rate or participate in collecting *DNA and plasma* for a $200 per subject reimbursement rate.

What procedures are required for specimen collection, processing and storage? During the informed consent process, the option to participate in the substudy will be discussed with the patient. The patient must consent to the POINT study in order to be eligible for the Biomarkers Ancillary study. The recently modified informed consent includes the Biomarkers study, with check boxes at the end of the form where subjects can consent to the ancillary study if they so choose. Once they provide consent to the main study and the substudy, a one-time sample of peripheral venous blood will be collected. Specimen collection kits, specimen labels, pre-paid shipping labels and shipping boxes will be shipped to all enrolling centers; details about the blood draw, including date and time of specimen collection, will be entered in WebDCU. No subject follow-up is required for the substudy.

For sites electing to participate in the *DNA specimen only* portion of the study, no processing will be required and specimens will be shipped at ambient temperature, express courier. Sites participating in *DNA and plasma collection* will need access to a centrifuge to separate the plasma from the red blood cells. The plasma will be aliquoted and frozen and the RBC's will be frozen until shipped. Both the plasma and RBC's will be shipped together on dry ice. All samples will be shipped express courier to the storage facility. A detailed specimen collection and processing manual, including shipping instructions, will be provided before the substudy starts up in August.

Contact Trese Biagini, POINT Clinical Research Nurse, at *Trese.Biagini@ucsfmedctr.org* or (415) 502-7307 with any questions about the above items.