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The Newsletter of the POINT Trial

Volume 2, Issue 3 3rd Quarter 2012

2012 3rd Quarter Recap

Retaining POINT Participants

Dear Colleagues,

As of September 30, there are 1105 participants enrolled, bringing us to 26.6% of our overall goal of 4150 participants enrolled in POINT. Of our 148 actively enrolling sites, 22 have not recruited any participants. If your site needs help with recruitment strategies, please let us know. Sites with study activity or enrollment temporarily suspended are also a missed opportunity and we hope to do everything possible to bring these sites back.

As important as it is to recruit participants, we understand that retaining them for the 90 days of the trial is also challenging. It's very important to encourage participants to complete the 90 days of the trial even if they come off study drug. The number of participants that are lost to follow-up (LTFU) continues to grow and the chart to the right shows that despite the latest protocol revisions, the numbers have increased in all three categories since June.

For new sites, and as a reminder to others, we want to emphasize the distinction between a participant *prematurely discontinuing use of study drug* and *withdrawing consent from the trial*. If participants discontinue study drug prematurely, we still want them to complete all follow-up visits, particularly their 90-day follow-up. All outcomes in the 90-day period count whether or not the participant is on study drug. Unless a participant informs us he or she has decided to withdraw consent, that participant is still part of POINT and should be followed through the 90 Day Follow-up Visit. The latest amendment expanded the window to 150 days from randomization to allow additional time for sites to contact hard-to-reach participants to minimize the number of participants that become designated as lost to follow-up.

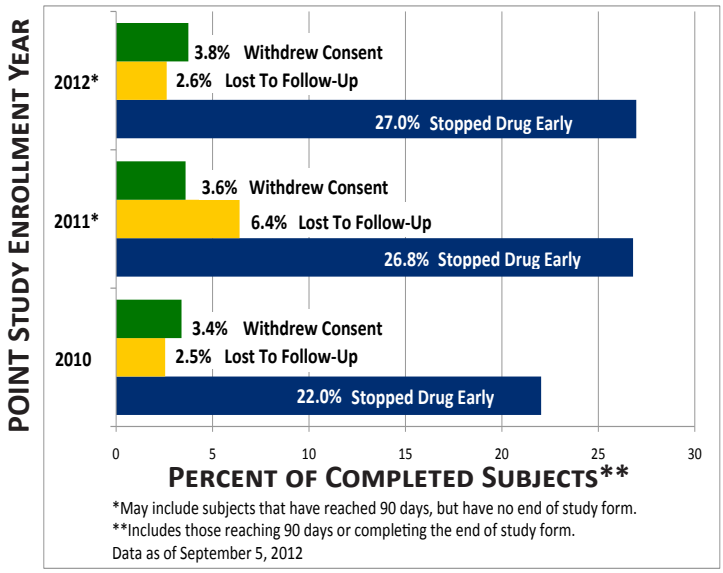
If a large number of participants are lost to follow-up during a clinical trial, it can greatly hamper interpretation of the results. Accordingly, the proportion of participants lost to follow-up is one of the quality and integrity indicators for randomized controlled trials.

Early communication between study coordinators and participants can help in encouraging participants through periods of uncertainty, reconsideration, and minor symptoms that get interpreted as side effects of study drug. Remind participants that stroke is a serious event, and we want to help them avoid it.

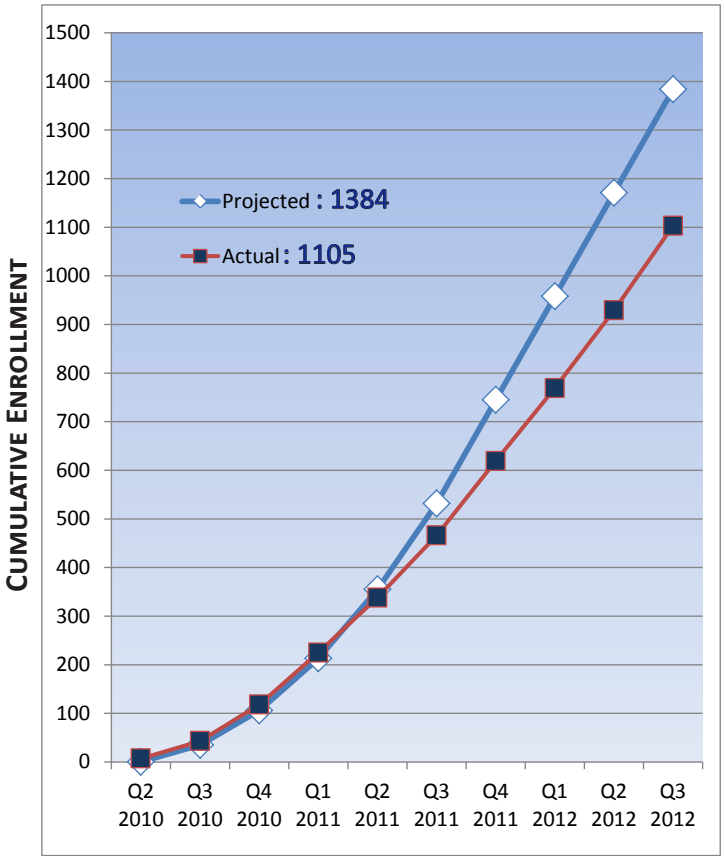
We know you're working hard. Please bring the hard work of recruitment home by communicating frequently with participants and encouraging them to complete this short trial.

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



POINT Cumulative Enrollment
May 2010 through Sept 2012



POINT Enrollment Update: Total=1105

In This Issue

THE COORDINATOR'S CORNER:
POINT INTERNATIONAL EXPANSION

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

POINT Frequently Asked Questions (FAQs)

Q. How can we continue to enroll subjects in POINT now that the Secondary Prevention of Small Subcortical Strokes (SPS3) Trial has reported that among patients with recent lacunar strokes, addition of clopidogrel to aspirin did not significantly reduce the risk of recurrent stroke and did significantly increase the risk of bleeding and death?

A. The result does not affect POINT and our DSMB continues to carefully monitor the safety and efficacy of this intervention in POINT. POINT is an acute trial while SPS3 was not.

The first FAQ in POINT addressed our justification for testing dual antiplatelet treatment in view of the MATCH trial results (and others) showing increased risk of hemorrhage in patients receiving dual treatment (see the detailed justification in FAQ 1.Q).

In brief, trials of clopidogrel in combination with aspirin after stroke/TIA suggest that the combination reduces the risk of stroke but increases the risk of major hemorrhage. However, in POINT we expect the risk of thrombosis to be high in the acute period after TIA and minor stroke and the risk of hemorrhage to be lower compared to the subjects with infarcts of moderate or large size enrolled in other trials (e.g., MATCH and SPS3). Thus, the combination of clopidogrel-aspirin may be particularly effective and relatively safe in patients with TIA and minor ischemic stroke.

Following its regular September 30, 2011 meeting, the POINT DSMB recommended that all sites encourage their subjects to use the lower dosage of aspirin daily, based on the interim results of the SPS3 and other trials. As per the protocol, POINT continues to recommend 162mg for the first 5 days and 81mg daily thereafter for the remaining 85 days.

A NOTE FROM WebDCU™

WebDCU™ shows a substantial number of outstanding forms and visits. Please help us get caught up. If you receive an email notification regarding "CRF Data Due or Open DCRs," "Visit Past Due," or "Screen Failure Log Past Due," please follow the steps in the email message to identify and resolve the issue(s).

IMPORTANT: For sites who are participating in the *POINT Biomarkers Ancillary Study*, WebDCU™ needs the Kit Shipping Information. Please update the [Project Spoke] table (Lines 7-12), being sure to include the kit recipient's address, name and phone number. The information currently listed for study drug shipping (Lines 13-20) should remain as is (unless there has been a change).

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

July-September Completed Readiness Calls *(listed alphabetically)*

Site (Hub)	City	State
Emory University Hospital Midtown (Emory)	Atlanta	GA
Essentia Health Duluth (Minnesota)	Duluth	MN
Norton Brownsboro Hospital (Kentucky)	Louisville	KY
Norton Hospital (Kentucky)	Louisville	KY
SUNY Downstate (CRC)‡	Brooklyn	NY
United Hospital (Minnesota)	St. Paul	MN

‡ Has 1 or more enrollment

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

Site (Hub)	City	State	#
Guilford Neurologic (CRC)	Greensboro	NC	69
Hospital of UPenn (UPenn)	Philadelphia	PA	44
Detroit Receiving (Wayne)	Detroit	MI	28
Henry Ford (HFHS)	Detroit	MI	24
OHSU - Oregon (OHSU)	Portland	OR	23
University of Kentucky (Kentucky)	Lexington	KY	23
Kaleida (CRC)	Buffalo	NY	21
Mayo Arizona (CRC)	Phoenix	AZ	21
Memorial Hermann (UT Houston)	Houston	TX	21
Beaumont Royal Oak (Wayne)	Royal Oak	MI	21
Advanced Neuro Specialists (CRC)	Great Falls	MT	21
Colorado Neuro Institute (CRC)	Englewood	CO	19
Cleveland Clinic (CRC)	Cleveland	OH	19
Abington (UPenn)	Abington	PA	18
Allegheny General Hospital (CRC)	Pittsburgh	PA	18
NYP Columbia (NYP)	New York	NY	18
Temple Univ Hospital (Temple)	Philadelphia	PA	18
Mission Hospital (CRC)	Asheville	NC	16
Palmetto Health Richland (CRC)	Columbia	SC	16
Regions Hospital (Minnesota)	St. Paul	MN	16

Sites with 11-15 subjects enrolled:	15
Sites with 6-10 subjects enrolled:	32
Sites with 1-5 subjects enrolled:	74
Sites with 0 subjects enrolled:	22

COORDINATOR'S CORNER

POINT International Expansion

by Rebecca Stewart, POINT Operations and International Specialist

International study teams will soon join the POINT Trial to increase participant recruitment and enrollment.

Work is currently underway to expand POINT outside of the United States. During the past year, the POINT CRC and UCSF POINT CCC have conducted preliminary research into regulatory and logistic requirements for international expansion. Over sixty sites across ten countries were polled to determine their interest in the study and the feasibility of recruiting for POINT in various regions. After extensive review of this data, approval for the expansion has been received from both the study DSMB and the Fogarty International Center at the National Institutes of Health.

The CRC will work closely with partner groups Harrison Clinical Research and Neuroscience Trials Australia for international site management and monitoring. The expansion will initially include sites in Canada and Australia/New Zealand, with the United Kingdom and Taiwan to follow. Other partners and countries may be added in the coming months.

Dr. Shelagh Coutts at the University of Calgary, Dr. Bernard Yan at the Australasian Stroke Trials Network, Dr. James Kennedy at the University of Oxford, Dr. Ana Roldan at the University of British Columbia, Dr. Chung Hsu at the China Medical University Healthcare System, and Dr. Natan Bornstein at the Tel-Aviv Sourasky Medical Center have all been instrumental in identifying potential sites and assisting with the preliminary requirements for their respective regions. The first international participant should be enrolled early in 2013.

Please feel free to contact Rebecca Stewart, POINT CRC Operations and International Specialist, at ***rstewart@emmes.com*** or (301) 251-1161 extension 2773 if you have any questions about the above items.