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The Newsletter of the POINT Trial

Volume I, Issue IV 3rd Quarter 2011

2011 3rd Quarter Recap

Early Enrollment Milestone of 10% Met

Dear Colleagues,

With the randomization on August 29, 2011 of the **415th subject** at Allegheny General Hospital in Pittsburgh, PA, we met an early enrollment milestone of 10% of our overall goal of 4150 subjects in POINT. Nice work, everyone.

Secondary Prevention of Small Subcortical Strokes (SPS3) Trial: Don't Worry
The Secondary Prevention of Small Subcortical Strokes (SPS3) Trial is a randomized, multicenter, international clinical trial designed to test whether a combination of aspirin and clopidogrel would be more effective than taking aspirin alone as a means to prevent a recurrent stroke in patients who had a subcortical stroke. As many of you are already aware, in July of this year, the National Institute of Neurological Disorders and Stroke (NINDS) stopped the combination antiplatelet intervention in the trial, acting on the recommendation of the study's Data and Safety Monitoring Board (DSMB).

The decision of the NINDS does not affect the POINT Trial, and our DSMB continues to carefully monitor the safety and efficacy of the intervention in POINT. Trials of clopidogrel in combination with aspirin after stroke and TIA suggest that the combination reduces risk of stroke but increases risk of major hemorrhage. 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 high severity enrolled on other trials. In patients with TIA and minor stroke, such as those enrolled in POINT, the combination of clopidogrel and aspirin may be particularly effective and relatively safe.

We've prepared a detailed FAQ in response to the stopping of the antiplatelet arm of SPS3, which is included in this newsletter (see page 2) and uploaded to the FAQ section of the POINT NETT site, available here: http://sitemaker.umich.edu/nett/point_faqs. Please don't hesitate to contact us directly if you have questions or require more information.

Looking Ahead: Q4 2011
We're in the last quarter of 2011, and we thought it'd be a good opportunity to revisit our site activation and subject enrollment goals for the last 3 months of this year. At the end of the third quarter of 2011, there were **127 sites ready to enroll in POINT**; 94 of those sites had 1 or more enrollments, with **466 subjects enrolled by the end of September**. Our year-end targets are 150 activated sites and 745 enrollments. We're certain we will achieve our target number of activated sites this year. In order to reach our 2011 target enrollment of 745, **we need an additional 279 enrollments**. Impossible? Not if each of the 127 activated sites enrolls 1 subject per month for the rest of the year. We know it can be done, we appreciate your dedication, and we look forward to working with you to meet — and possibly exceed — this enrollment target!

Keep up the great work, and thanks again.

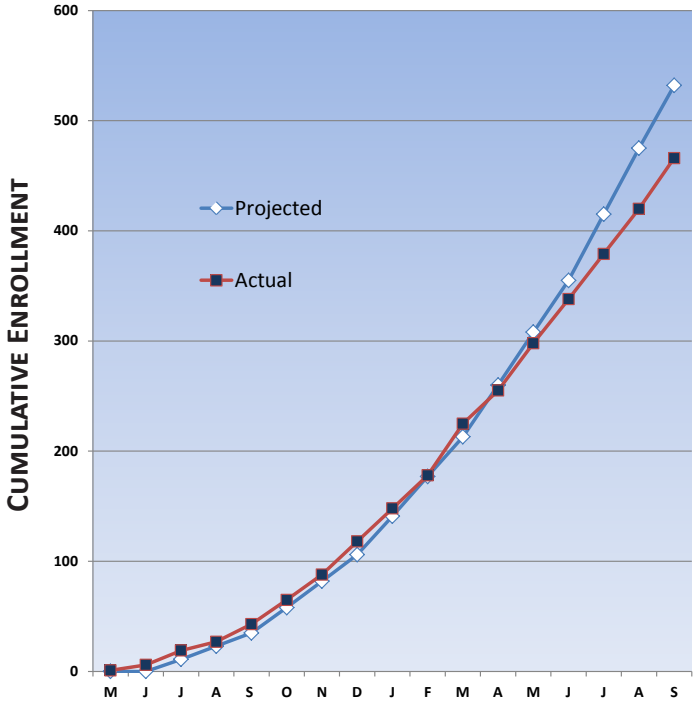
Sincerely,

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 September 2011



POINT Enrollment Update: Total=466

Top Enrollers (as of September 30, 2011)

Site (Hub)	City	State	#
Guilford Neurologic (CRC)	Greensboro	NC	44
Hospital of UPenn (UPenn)	Philadelphia	PA	24
Detroit Receiving (Wayne)	Detroit	MI	18
Henry Ford (HFHS)	Detroit	MI	17
University of Kentucky (Kentucky)	Lexington	KY	16
Mayo Arizona (CRC)	Phoenix	AZ	12
Froedtert Mem. Hosp (Wisconsin)	Milwaukee	WI	12
Colorado Neuro Institute (CRC)	Englewood	CO	11
OHSU - Oregon (OHSU)	Portland	OR	11
Advanced Neurology Specia (CRC)	Great Falls	MT	10
Beaumont Royal Oak (Wayne)	Royal Oak	MI	10
Hennepin County Med. Ctr (MN)	Minneapolis	MN	10
Abington (UPenn)	Abington	PA	9
Emory (Emory)	Atlanta	GA	9
Palmetto Health Richland (CRC)	Columbia	SC	9
Allegheny General Hospital (CRC)	Pittburgh	PA	8
Bon Secour (CRC)	Midlothian	VA	8
Intercoastal Medical (CRC)	Sarasota	FL	8
Northwestern University (CRC)	Chicago	IL	8
Temple Univ Hospital (Temple)	Philadelphia	PA	8
El Camino (Stanford)	Mountain View	CA	7
GA Health Sciences - MCG (CRC)	Augusta	GA	7
University Hospital (Cincinnati)	Cincinnati	OH	7
Sinai - Grace Hospital (Wayne)	Detroit	MI	7
York (UPenn)	York	PA	7
Sites with 1-6 subjects enrolled			69

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 National Institute of Neurological Disorders and Stroke (NINDS) has stopped the dual antiplatelet intervention (clopidogrel and aspirin) in the Secondary Prevention of Small Subcortical Strokes (SPS3) Trial?

A. This decision does not affect POINT and our DSMB is carefully monitoring the safety and efficacy of this intervention in POINT.

The first POINT FAQ addressed our justification for testing dual anti-platelet treatment in view of the MATCH trial results (and others) showing increased risk of hemorrhage in patients receiving dual treatment (see detailed justification in FAQ #1 at http://sitemaker.umich.edu/nett/point_faqs). In brief, trials of clopidogrel in combination with aspirin after stroke/TIA suggest that the combination reduces risk of stroke but increases risk of major hemorrhage. However, 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 high severity enrolled in other trials. Thus, the combination of clopidogrel-aspirin may be particularly effective and relatively safe in patients with TIA and minor ischemic stroke.

For a complete list of the FAQs, please visit the NETT website: https://sitemaker.umich.edu/nett/point_faqs

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

Site (Hub)	City	State
Austin Brackenridge (Texas)‡	Austin	TX
Austin Seton MC (Texas)	Austin	TX
Benaroya (CRC)	Seattle	WA
BWMC (Maryland)	Baltimore	MD
Christ Hospital (Cincinnati)‡	Cincinnati	OH
Frankford (Temple)‡	Philadelphia	PA
Jeanes (Temple)	Philadelphia	PA
Methodist Hosp Houston (CRC)	Houston	TX
NAI Henrico - Forest (CRC)	Richmond	VA
NAI Henrico - Parham (CRC)	Richmond	VA
Northshore - Evanston (CRC)	Evanston	IL
Northshore - Glenview (CRC)	Glenview	IL
Ohio State Univ Med Ctr (CRC)	Columbus	OH
Queens Med Ctr (CRC)	Honolulu	HI
Sutter General (CRC)	Sacramento	CA
Sutter Memorial (CRC)	Sacramento	CA
UCSD Hillcrest (CRC)	San Diego	SD
Univ FL - Jacksonville (CRC)*	Jacksonville	FL

‡ Has 1 or more enrollment as of September 30, 2011
* Activated June 30, 2011

COORDINATOR'S CORNER

Best Practices in Participating in and Documenting the Informed Consent Process: Reflections from Site Monitoring Visits

by Carolyn Burke, Project Manager at the CRC, Andrace Deyampert and Shirley Frederiksen, Project Monitors at the NETT

The POINT Site Monitoring Team, comprised of monitors from the NETT and POINT-CRC, conducts initial monitoring visits at sites that have at least two randomized subjects who have completed the 90 day study visit. As of the end of September, a combined total of 38 site monitoring visits have been conducted. A review of observations from these site visits has revealed some practices that may make sites vulnerable to consent–based protocol violations. Based on those observations, and in support of regulatory compliance and best practices in the informed consent process, we offer the following reminder:

1) Ensure the appropriate consent document is submitted to the IRB for review/approval and subsequently incorporated into the site Essential Document Collection (WebDCU)

The recent amendment to the protocol (version 3) resulted in corresponding modifications to the ICF and many sites are submitting continuing/annual review materials to their IRB. Some institutions require study teams to modify informed consent documents to include institutionally standardized language. Such modifications should be reviewed by the appropriate partner, either NETT or CRC staff, to ensure the modifications do not reflect substantive changes to the intent of the information provided to potential study subjects documents.

2) Ensure the subject receives the complete, current, IRB-approved consent form.

The majority of enrollments for POINT are identified through the Emergency Room, an urgent care facility, or through other acute care environments. In such fast-paced environments, it is important to take a few minutes to ensure you have the current approved version of the ICF, complete with all pages, to review with potential subjects.

3) Ask the subject to initial each page of the consent form.

Each institution's IRB has its own requirements regarding whether a line for a subject's initials must appear on each page of the informed consent document. Obtaining a subject's initials on each page of the consent form documents that the subject received each page and supports best practices in Good Clinical Practice (GCP) in obtaining a subject's consent.

4) Include a written summary of the consent process in the research or medical files.

Per 21 CFR 312.62 (b), "the case history for each individual shall document that informed consent was obtained prior to participation in the study." To ensure you've supplied such a case history for your site's study files, include a written description of the process you used to obtain the consent, including a discussion of the risks and benefits, and the voluntary nature of participation in the subject's research or medical file.

5) Document staff authorized to facilitate the consent discussion.

It is important that the individual facilitating the consent process is a study team member with the appropriate expertise to discuss the study and address questions and concerns posed by subjects. Though it is the primary responsibility of the site PI to ensure the consent process at each site is consistent with human subject's protection regulations and safeguards, the PI may also delegate this responsibility to other site team staff. Such authorizations should be appropriately and consistently noted on the site Delegation of Authority Log. All staff facilitating the consent process are responsible for making sure the subject/LAR provides a signature, date and time (if required by your IRB) in the designated areas on the ICF.

In remembering the steps above and ensuring due diligence in facilitating and documenting each component of the informed consent process, you can be confident you've appropriately implemented the process and offered the candidate an opportunity to make an informed decision about participation in the POINT study.