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The Newsletter of the POINT Trial

Volume 2, Issue 4 4th Quarter 2012

2012 4th Quarter Recap

Looking Back on the Year

Dear Colleagues,

As of the end of 2012, there are 1249 subjects enrolled in the POINT Trial, bringing us to 30% of our overall goal of 4150 subjects. Of our 150 actively enrolling sites, 144 sites have at least 1 enrollment. 13 subjects have been enrolled in the Biomarker substudy with 7 subjects from CRC sites and 6 subjects from NETT sites.

Expansion of POINT to international sites is progressing on schedule, with Canada and Australia gearing up to activate sites starting in January.

The 2013 International Stroke Conference takes place in Honolulu, February 6-8. The POINT Poster Session is scheduled for Wednesday, February 6th from 4:45pm to 5:15pm. Find us at Poster Board Number P119. Raffle tickets will be handed out during the poster session. Visit the POINT poster and pick up your raffle ticket for a chance to win neurological exam tools, including a ***Golden Trömner Reflex Hammer!***

The poster session is an excellent opportunity to meet fellow study team members, review study progress, and ask questions of us in person. We hope to see you there!

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

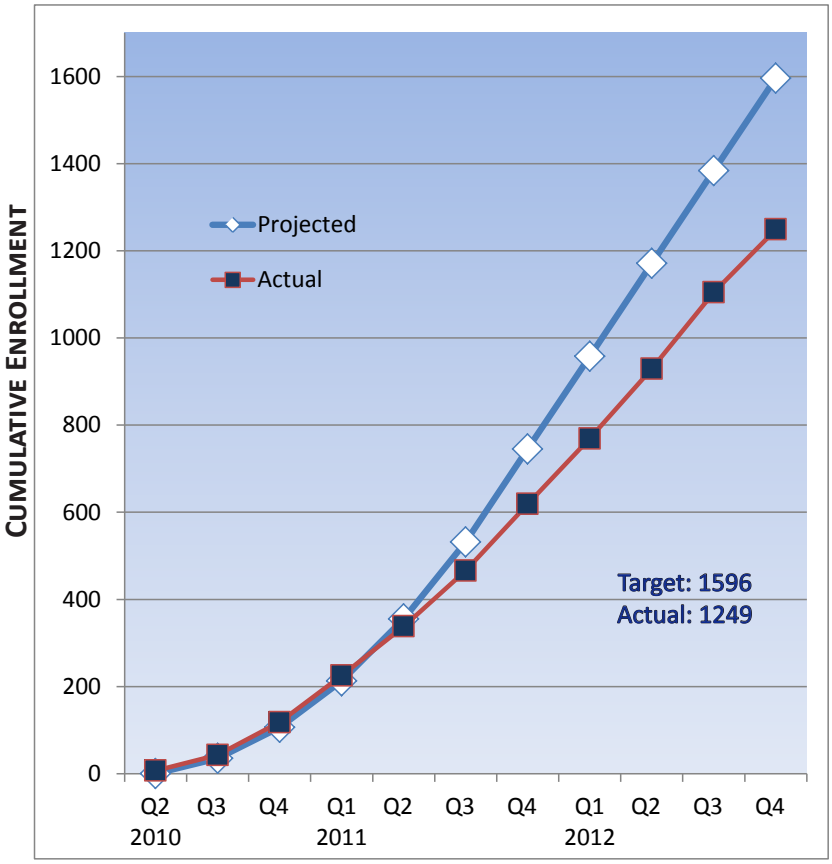
Sincerely,

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

In This Issue

THE COORDINATOR'S CORNER:
POINT INTERNATIONAL EXPANSION

POINT Cumulative Enrollment
May 2010 through December 2012



POINT Enrollment Update: Total=1249

October-December Completed Readiness Calls

Site (Hub)	City	State
Jefferson Hospital (Temple)	Philadelphia	PA
Medical Univ of South Carolina (Cincinatti)	Charleston	SC

Top Enrollers ***(as of December 31, 2012)***

Site (Hub)	City	State	#
Guilford Neurologic (CRC)	Greensboro	NC	72
Hospital of UPenn (UPenn)	Philadelphia	PA	51
Detroit Receiving (Wayne)	Detroit	MI	30
Henry Ford (HFHS)	Detroit	MI	27
OHSU - Oregon (OHSU)	Portland	OR	25
Mayo Arizona (CRC)	Phoenix	AZ	24
University of Kentucky (Kentucky)	Lexington	KY	24
Advanced Neurology Specialists (CRC)	Great Falls	MT	23
Beaumont Royal Oak (Wayne)	Royal Oak	MI	23
Abington (UPenn)	Abington	PA	22
Memorial Hermann (UT Houston)	Houston	TX	22
Regions Hospital (Minnesota)	St. Paul	MN	22
Kaleida Stroke Center (CRC)	Buffalo	NY	21

Sites with 16-20 subjects enrolled: 9
Sites with 11-15 subjects enrolled: 17
Sites with 6-10 subjects enrolled: 39
Sites with 1-5 subjects enrolled: 66
Sites with 0 subjects enrolled: 26

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

POINT Frequently Asked Questions (FAQs)

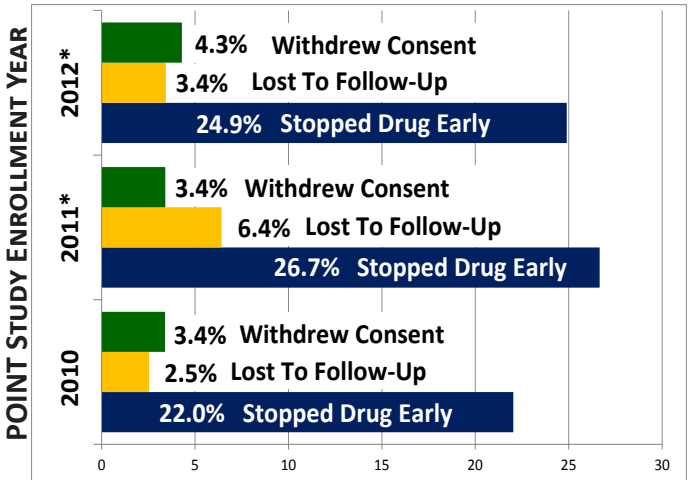
Q. A subject ingested the loading dose of study drug and vomited shortly thereafter. She said if she ingested a little food she could take the pills again and keep them down. Should we reload her with 8 more pills?

A. No. This has been a rare occurrence in POINT. A subject may vomit immediately and all of the study pills are visible in the vomitus. Others may vomit a variable time after ingestion and the pills are more or less visible. Sometimes the pills have dissolved but may or may not have been absorbed. Finally, each subject receives exactly 97 study pills necessary to complete the trial. Therefore, when all risks and benefits for the subjects and the POINT trial are taken into account, reloading should not occur.

Q. Several IRBs have asked questions about whether the FDA has approved clopidogrel, aspirin, or the combination of clopidogrel and aspirin for patients with TIA, rather than ischemic stroke; and, is the clopidogrel loading-dose of 600 mg approved. Can POINT provide guidance in answer to these queries?

A. Clopidogrel is approved by the FDA for use after ischemic stroke, but is not approved specifically for use after TIA. Consequently, neither is the combination of clopidogrel plus aspirin approved by the FDA. Clopidogrel is one of the antiplatelet drugs recommended by the American Stroke Association/American Heart Association and all other major USA and European guidelines. The purpose of the POINT trial is to determine if clopidogrel plus aspirin is more beneficial than aspirin alone in this population at high risk for thrombosis and presumably low risk for serious hemorrhage, because they have minimal brain damage. In addition, 300-600 mg is the current loading-dose recommendation by the American College of Cardiology/American Heart Association for acute coronary syndrome, an atherothrombotic disorder akin to acute TIA and minor ischemic stroke. There is no recommendation for acute minor brain ischemia and therefore POINT is being conducted.

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 December 14, 2012

The FDA status on aspirin is contained in its Final Rule: "The agency believes a dose of 50 to 325 mg is an effective daily dose for subjects with TIA or cerebral ischemia. Therefore, in this final rule, the agency is providing for a dosage of 50 to 325 mg aspirin daily (http://www.fda.gov/ohrms/dockets/98fr//102398c.txt)." The FDA is silent on clopidogrel for TIA as noted above, but all stroke prevention guidelines recommend aspirin, clopidogrel, or aspirin plus dipyridamole for prevention of stroke in patients after cerebral ischemia (stroke or TIA).

The FDA reviewed a summary of the POINT trial and waived any requirement for a New Drug Application (IND). If a site chooses to include this information in its consent form, they certainly may do so.

There were 1220 subjects enrolled in POINT when the NIH-appointed Data Safety Monitoring Board met on October 12, 2012 and concluded, "As no safety concerns were identified, the POINT trial should proceed as planned."

A Note From WebDCU™

There will be a database freeze in March to generate the DSMB report. Please respond to open DCRs, address rule violations, and enter visits and CRFs promptly in WebDCU™. Queries and unresolved rule violations on CRF 19 (SAE/Clinical Outcome Reporting Form) can hold up the adjudication process, so these are of particular importance.

Also, please note that subjects that have not been reached after 150 days from randomization should be declared Lost to Follow Up.

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

COORDINATOR'S CORNER: POINT International Expansion

by Rebecca Stewart

Please join us in welcoming international study teams to the POINT Trial!

Ethics committee applications have been submitted for sites in Australia, New Zealand, and Canada, and study teams in each of these countries have been working closely with the POINT CRC to complete site activation requirements for the study. Communication continues with research groups in the United Kingdom and Taiwan. A total of 40 new sites are expected from this initial effort. Kudos to the WebDCU™ team for preparing the website for international involvement!

Working with international sites on their regulatory submissions can be challenging because processes differ by country. The application process for Canada, for example, is similar to the US with a country-level approval of the study being required in addition to local ethics committee approvals for each site. By contrast, in Australia, a single site serves as "lead" for the entire country and submits the initial application; subsequent approvals for additional sites are then linked to the lead site.

The new study teams are excited to join POINT and look forward to contributing to enrollment efforts. The first international sites should be activated within the next month.

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.