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The Newsletter of the POINT Trial

Volume 2, Issue 1 1st Quarter 2012

2012 1st Quarter Recap

Site Activation Milestone of US Sites Met

Dear Colleagues,

We've met and exceeded our target of 150 US sites at the end of the first quarter of 2012 with 151 activated sites ready to enroll in POINT! 126 of those sites have at least 1 enrollment, and with the 769th subject enrolled on March 31, 2012, at Palmetto Health Richland in Columbia, SC, we are at 18.5% of our overall goal of 4150 subjects enrolled in the POINT Trial.

March turned out to be our best month so far with a new record of 59 enrollments! Expansion to OUS sites is in the works and we'll keep you updated as that progresses.

Stopping Study Drug versus Stopping the Study

We'd like to remind investigators and study personnel that premature study drug discontinuation is different from a subject deciding to stop participating in the POINT Trial. Distinguishing this difference is important; we want to minimize the number of subjects in POINT for whom data are incomplete. Considering the efforts made to recruit subjects into POINT, we want to encourage subjects to complete the 90 days of the trial as best we can. All outcomes in the 90-day period count, whether or not the subject is on study drug. Unless a subject lets us know he or she has decided to stop participating in the trial and withdraws consent, that subject should be followed through the 90 Day Follow Up Visit.

Platelet Assays - Why They Shouldn't Be Done on POINT Enrollments

The use of Platelet Function Tests as a means of monitoring the presence and effectiveness of antiplatelet medications poses an issue in POINT due to the potential for unblinding. Assays for clopidogrel effects on platelets are strictly prohibited. To highlight the importance of maintaining POINT as a double-blind trial as well as address the use of platelet function assay results for modifying aspirin dosing for POINT subjects, we've prepared an FAQ 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*.

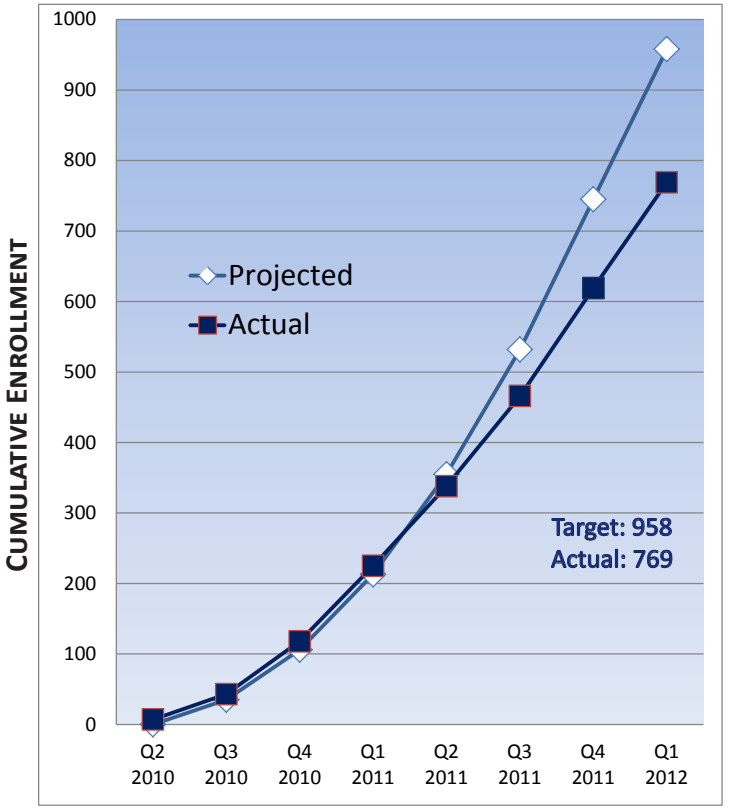
Please don't hesitate to contact us directly if you have questions or require more information. We're off to a great start in 2012, thanks to everyone's continued hard work.

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 March 2012



POINT Enrollment Update: Total=769

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

Site (Hub)	City	State	#
Guilford Neurologic (CRC)	Greensboro	NC	58
Hospital of UPenn (UPenn)	Philadelphia	PA	32
Detroit Receiving (Wayne)	Detroit	MI	22
Henry Ford (HFHS)	Detroit	MI	21
University of Kentucky (Kentucky)	Lexington	KY	19
Advanced Neurology Specia (CRC)	Great Falls	MT	18
Colorado Neuro Institute (CRC)	Englewood	CO	17
Beaumont Royal Oak (Wayne)	Royal Oak	MI	16
OHSU - Oregon (OHSU)	Portland	OR	16
Mayo Arizona (CRC)	Phoenix	AZ	15
Memorial Hermann (UT Houston)	Houston	TX	14
Abington (UPenn)	Abington	PA	13
Kaleida (CRC)	Buffalo	NY	13
Palmetto Health Richland (CRC)	Columbia	SC	13
Froedtert Mem. Hosp (Wisconsin)	Milwaukee	WI	12
NYP-Columbia (NYP)	New York	NY	12

Sites with 10-11 subjects enrolled:	11
Sites with 6-9 subjects enrolled:	16
Sites with 1-5 subjects enrolled:	83
Sites with 0 subjects enrolled:	25

POINT Frequently Asked Questions (FAQs)

Q. Is Effexor a prohibited or discouraged medication in POINT?

A. Effexor (venlafaxine) is in a class of medications called selective serotonin and norepinephrine reuptake inhibitors (SNRIs). From the perspective of the POINT trial, **this class of drug is neither prohibited nor discouraged.** Under Precautions, rather than Contraindications or Warnings, the Effexor label states, "Abnormal Bleeding: SSRIs and SNRIs, including Effexor, may increase risk of bleeding events. Concomitant use of aspirin, nonsteroidal anti-inflammatory drugs, warfarin, and other anticoagulants may add to this risk. Patients should be cautioned about the risk of bleeding associated with concomitant use of Effexor and NSAIDs, aspirin, or other drugs that affect coagulation." There may be other drugs that carry this precaution. POINT encourages its enrolling sites to consider the risk-benefit for individual patients of concomitant use of serotonin reuptake inhibitors/serotonin norepinephrine reuptake inhibitors and study drug before enrolling patients.

Q. Is it ok to obtain platelet function assays on POINT subjects?

A. No. All subjects should be on aspirin and there is no compelling evidence to support modifying aspirin dosing based on the results of platelet function tests. Assays for clopidogrel effects on platelets are strictly prohibited, as this is a double-blind trial and platelet function testing can unblind the study drug.

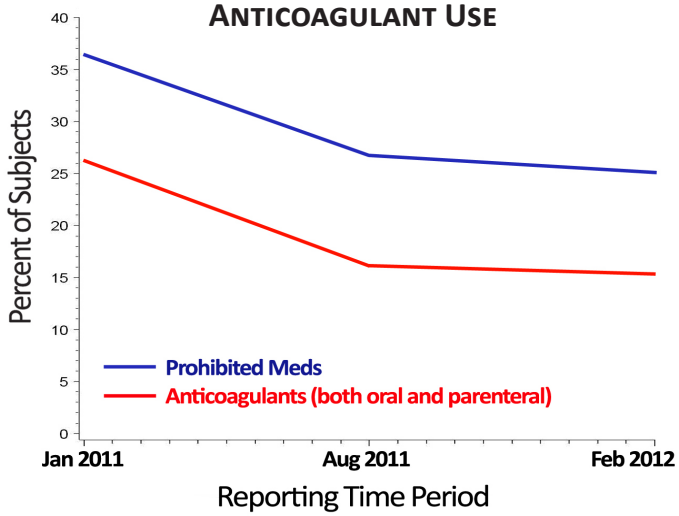
Q. In the case of a patient with blindness that precedes the onset of a minor ischemic stroke that causes the patient to be considered for POINT, is it necessary to add 3 points for blindness in the NIHSS as this will exclude the patient?

A. Yes, this patient must be excluded. The rationale is that a blind subject could experience a large occipital lobe infarction that is clinically silent. The NIHSS is a tried-and-true validated instrument that we do not want to modify just for POINT. In the case of a patient with blindness that precedes the onset of a TIA, eligibility is left to the judgment of the investigator. If the patient is otherwise in good neurologic health such that future neurologic assessments will likely be reliable, enrollment is allowable.

January-March Completed Readiness Calls *(listed alphabetically)*

Site (Hub)	City	State
AFIME Research Group (CRC)	Verona	NJ
Carolinas Neuroscience & Spine Inst (CRC)‡	Charlotte	NC
Massachusetts General Hospital (CRC)	Boston	MA
MetroHealth (CRC)‡	Cleveland	OH
Neurology Center of Shelby (CRC)‡	Shelby	NC
Parkland Health & Hospital System (CRC)	Dallas	TX
Regions Hospital (University of Minnesota)‡	St Paul	MN
Ridgeview Med Ctr (University of Minnesota)	Waconia	MN
SUNY Upstate Medical University (CRC)‡	Syracuse	NY
Two Twelve Med Ctr (University of Minnesota)	Waconia	MN
UAB Comprehensive Stroke Center (CRC)‡	Birmingham	AL
University of Illinois Medical Center (CRC)	Chicago	IL
University of Iowa (CRC)	Iowa City	IA
UT Southwestern Hospital System (CRC)	Dallas	TX
Washington Hospital (Maryland)‡	Washington	DC

‡ Has 1 or more enrollment



The decreasing use of prohibited medications, particularly anticoagulants, reflects the substantial effect of our continued efforts. Let's keep this trend going in this direction!

COORDINATOR'S CORNER

Important Reminders from WebDCU

by Aaron Perlmutter, POINT Data Manager

• A Main Menu Alert is being added to notify sites when a subject has finished the study and a SAE/Clinical Outcome still requires follow up. If you receive this alert, please update the *SAE/Clinical Outcome eCRF* (Form 19) accordingly.

Compare Study IDs at randomization:
Remember to print and bring the *Randomization Verification Form* to the pharmacy to verify that the study drug ID on the form assigned by WebDCU and listed on the form matches the study drug ID on the bottle retrieved from the pharmacy.

• The link to the *Randomization Verification Form* (RVF) is included on the *Randomization eCRF* after it is submitted. The RVF should be filed in the subject record. See the latest Study Drug Handling At Site Template SOP here: *https://sitemaker.umich.edu/nett/point_toolbox*

• Outcome Event Visits should be completed any time a subject experiences an Outcome Event (ischemic stroke, TIA, or myocardial infarction).

24-Hour WebDCU RANDOMIZATION EMERGENCY Hotline:

1-866-450-2016

A new WebDCU Randomization Emergency Hotline (1-866-450-2016) has been established for emergency randomization issues only. Please use this number if you encounter problems trying to randomize in WebDCU or if there is a problem with the randomization assignment generated by WebDCU.

• The *Concomitant Medications eCRF* (Form 18) should list only the prohibited and discouraged medications that were taken by the subject since the subject's last visit, whether it was the Baseline/Randomization, 7 Day Follow up, Outcome Event, or 90 Day Follow Up.

Contact Aaron Perlmutter, POINT Data Manager, at *perlmutt@musc.edu* or (843) 876-1261 with any questions about the above items.