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The Newsletter of the POINT Trial

Volume 3, Issue 1 1st Quarter 2013

2013 1st Quarter Recap

ISC, February, 2013

Dear Colleagues,

Enrollment Update

In the first quarter of 2013, 135 subjects were enrolled in the study, with March the strongest month of the quarter with 50 enrollments. With 1384 enrollments so far, we're at 33% of our target enrollment of 4150 subjects; currently, 152 sites are actively enrolling subjects. Expansion of the study to international sites is taking longer than originally projected; the first sites outside the US are expected to begin enrolling subjects in April.

2013 International Stroke Conference: CHANCE

As many of you are aware, the results of the CHANCE Trial were presented at the 2013 International Stroke Conference in Hawaii in February of this year. CHANCE, which stands for **C**lopidogrel in **H**igh-Risk Patients with Acute Non-disabling **C**erebrovascular **E**vents, enrolled 5170 subjects in China with high-risk TIA and minor ischemic stroke using eligibility criteria similar to those of POINT. CHANCE is the first trial to suggest that the combination of aspirin and clopidogrel is safe to use in patients with ischemic stroke or TIA.

There are important differences between the CHANCE and POINT trials, which are described on page 2 of the newsletter. The POINT informed consent form (ICF) has been modified in light of the CHANCE results, and you'll find the revised language on page 2 as well.

The POINT DSMB is fully aware of the CHANCE results and continues to monitor POINT carefully. In preparation for the POINT DSMB meeting in May, all POINT data are being updated. The DSMB and NIH will discuss the pre-planned first interim analysis results at their meeting on May 2, 2013. Meanwhile, the DSMB has recommended that the POINT trial continue per its current protocol.

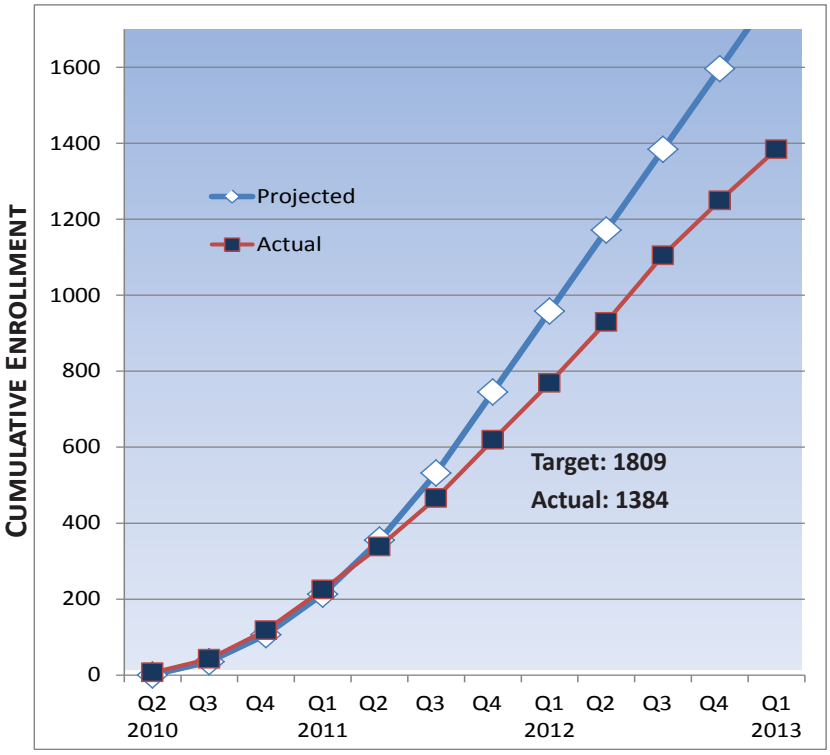
As always, please don't hesitate to contact us directly if you have questions or require more information.

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

In This Issue

POINT Cumulative Enrollment

May 2010 through March 2013



POINT Enrollment Update: Total=1384

New Sites January-March

Site (Hub)	City	State
Cooper U. Hospital (UPenn)	Camden	NJ
Barnes Jewish Hospital (U. of Cincinnati)	St. Louis	MO
Ben Taub Gen. Hospital (U. of TX)	Houston	TX
St. John Hospital (Wayne State)	Detroit	MI
Southern CA Permanente Group (CRC)	Los Angeles	CA
University of Colorado (CRC)	Aurora	CO

***Top Enrollers** (as of March 31, 2013)*

Site (Hub)	City	State	#
Guilford Neurologic (CRC)	Greensboro	NC	74
Hospital of UPenn (UPenn)	Philadelphia	PA	58
Detroit Receiving (Wayne)	Detroit	MI	31
Henry Ford (HFHS)	Detroit	MI	28
Mayo Arizona (CRC)	Phoenix	AZ	27
OHSU - Oregon (OHSU)	Portland	OR	26
Temple Univ. Hospital (Temple)	Philadelphia	PA	26
Methodist Hospital (CRC)	Houston	TX	26
Beaumont Royal Oak (Wayne)	Royal Oak	MI	25
University of Kentucky (Kentucky)	Lexington	KY	25
Memorial Hermann Hospital (UPenn)	Philadelphia	PA	25
Regions Hospital (U. of MN)	St. Paul	MN	24

Sites with 16-23 subjects enrolled: 17
Sites with 11-15 subjects enrolled: 13
Sites with 6-10 subjects enrolled: 41
Sites with 1-5 subjects enrolled: 69
Sites with 0 subjects enrolled: 20

CHANCE: Clopidogrel in High-Risk Patients with Acute Non-disabling Cerebrovascular Events

CHANCE and POINT

There are important differences between the CHANCE and POINT trials, including:

- **secondary prevention practices**: rates of untreated hypertension, diabetes and dyslipidemia are higher in China than US
- **enrollment window**: 24 hours in CHANCE, 12 in POINT
- **loading dose**: 600mg in POINT compared to 300mg in CHANCE
- **demographics**: one-third of the enrollments in CHANCE are women, compared to 50% in POINT
- **length of dual anti-platelet intervention:** 90 days in POINT versus 21 days in CHANCE
- **intracranial atherosclerosis:** more frequent in China

Antiplatelet therapy may be more effective in this subgroup. In addition, Chinese are more likely to have genetic polymorphisms that reduce clopidogrel's efficacy, so antiplatelet effects could be greater in those of European ancestry.

POINT Trial Informed Consent

The POINT informed consent form (ICF) has been modified in light of the CHANCE results, and the appropriate wording has been added to provide full and balanced disclosure. The text includes: "A single trial in China studying patients with stroke and TIA suggested that the combination of clopidogrel and aspirin was safe and effective. However, there are differences in the treatment of patients, the types of stroke, and the design of the trial, so it is not clear whether these results would apply to you." This new content has been provided to all sites for inclusion in their forms, and for the consideration of their IRBs.

USING IPADS IN THE CONSENT PROCESS IN THE POINT TRIAL

A total of 120 sites will be receiving iPads over the next few months to aid in the consent process for the study. We urge you to encourage use of the iPads at enrolling sites so eligible patients can watch the consent video and better understand the POINT Trial. This should result in improved consent and retention rates.

Please let us know if you have any questions or concerns about using the iPads. We'd also like to know if you feel that these are helpful with the consent process.

Contact Tess Bonham (NETT)
tbonham@med.umich.edu or
Lloyd Henry (CRC)
crc@emmes.com
for more information.

Warning stickers will be placed on the back and front cover of the iPads to curb theft.

COORDINATOR'S CORNER: POINT Biomarker Ancillary Study Update

By Trese Biagini, RN

A brief summary of the POINT Biomarkers Ancillary Study for those of you new to POINT...

The POINT Biomarkers Ancillary Study began enrolling subjects in November 2012. Thanks to all of your hard work, the enrollment for the substudy is coming on strong with 58 subjects enrolled as of the first quarter of 2013. There were 20 enrollments in March, the highest enrolling month in the substudy so far. A total of 80 US sites are currently participating in the substudy, with 73 sites participating in *DNA and plasma*, and 7 sites participating in *DNA only*. Temple University (Temple) is the highest enrolling site to date with 7 enrollments, Methodist Hospital, Houston (CRC) is second with 5, and Hospital of the University of Pennsylvania (UPenn), Regions Hospital, St. Paul (University of Minnesota), St. Josephs's Regional Health Center (University of Texas, Houston) and University of Florida Health Sciences (CRC) are tied for third with 4 enrollments each.

This is the first systematic study of clopidogrel resistance in the setting of stroke prevention following TIA and minor ischemic stroke. A single blood specimen is collected from consented POINT participants at the time of enrollment for testing to determine inherited clopidogrel resistance. Per subject reimbursement varies 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.

We look forward to the Canadian and Australian sites coming on board soon. All OUS sites will be participating in collecting DNA and plasma.

Please feel free to contact Trese Biagini, POINT Clinical Research Nurse, at
trese.biagini@ucsf.edu or (415) 502-7307 if you have any questions about the above items.