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The Newsletter of the POINT Trial

Volume 3, Issue 4 4TH Quarter 2013

2013 4TH Quarter Recap

Dear Colleagues,

Happy New Year 2014!

Study Enrollment Update

We closed out 2013 with an enrollment of 1,883, reaching almost a third of our target of 5,840 subjects. The highest enrolling month in the quarter (and for the year) was October, with 63 enrollments. The fourth quarter also saw the first international enrollments at Canadian and Australian sites, with 22 new subjects outside the US. Eight new sites were activated this quarter, including more sites in Australia and Canada. New Zealand and the UK are not far behind! Welcome to all our new sites!

Discouraging Premature Study Drug Discontinuation

A substantial number of POINT subjects have prematurely and permanently discontinued study medication because of minor bleeding that they perceive to be drug-related. If a subject discontinues because of a severe nose bleed or other hemorrhage resulting in a physician visit and intervention, the decision is understandable and sensible. On the other hand, when a subject experiences mild skin bruising or hemorrhoidal bleeding, they generally should be encouraged to re-consider drug cessation. After all, the primary major risk is ischemic stroke and the commitment is for only 90 days. Aspirin is the cause of minor bleeds in other trials and may be in POINT; most subjects are likely to be prescribed aspirin if they discontinue study drug.

POINT ISC 2014: San Diego, CA

The UCSF POINT Clinical Coordinating Center will be hosting a reception for Principal Investigators and Study Coordinators during the International Stroke Conference (ISC) in San Diego, CA on February 12, 2014 at the Hilton Gaslamp Quarter (details on page 2). This is a great opportunity to meet POINT study team members, share enrollment ideas and discuss any study issues.

Invitations to the reception, including directions to the venue, have been sent out by email. Please let us know if you have not received the invitation, so you can RSVP.

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

Sincerely,

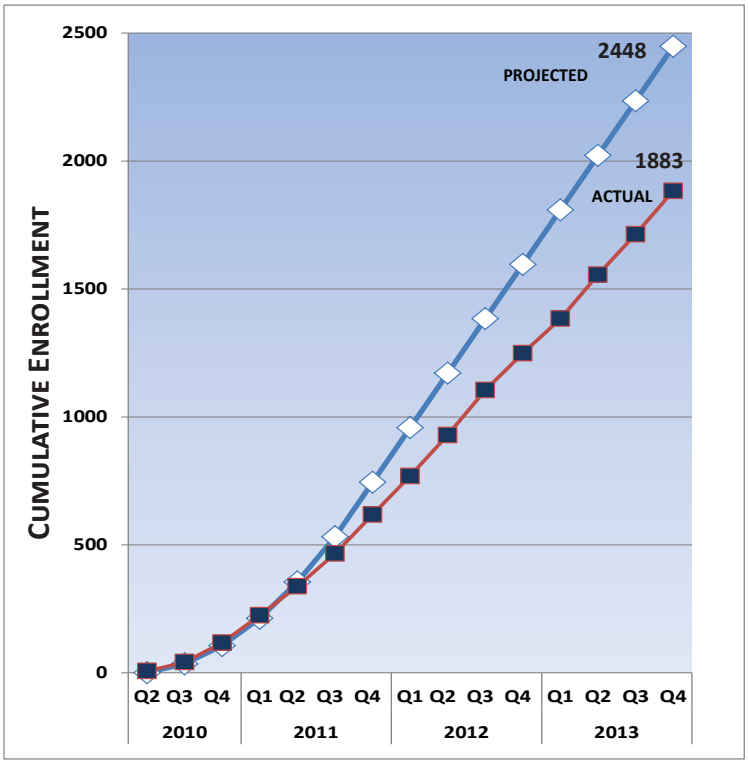
Clay Johnston MD, PhD, POINT Trial Principal Investigator

Don Easton MD, POINT Trial co-Principal Investigator

In This Issue: Preparing A Detailed Event Narrative, Competing Trials, Biomarker Study Enrollment Tips, and ISC 2014 Details

POINT Cumulative Enrollment

May 2010 through December 2013



POINT Enrollment Update: Total = 1883

Hot Enrollers for 3rd and 4th Quarter

Place	Subjects	Site (Hub)
1	12	University of Alberta (CRC), Hospital of UPenn (UPenn)
2	9	Wellspan York Hospital (CRC)
3	8	Guilford Neurological (CRC), Memorial Hermann (Texas), Columbia Univ. (NYP), Barnes Jewish Hospital (Cincinnati)
4	7	Stanford (UCSF), Advanced Neuro. Specialists (CRC), UMass Memorial Medical Center (CRC), Allegheny General (CRC)
5	6	University of Calgary, Foothills (CRC), Oregon Health & Science University (OHSU), Univ. of Florida (CRC), Cleveland Clinic, OH (CRC)

Top Enrollers (as of December 31, 2013)

Site (Hub)	City	State	#
Guilford Neurologic (CRC)	Greensboro	NC	83
Hospital of UPenn (UPenn)	Philadelphia	PA	76
OHSU- Oregon (OHSU)	Portland	OR	38
Memorial Hermann (Texas)	Houston	TX	35
Temple Univ. Hospital (Temple)	Philadelphia	PA	35
Advanced Neuro. Sp. (CRC)	Great Falls	MT	35
Detroit Receiving (Wayne)	Detroit	MI	34
Methodist Hospital (CRC)	Houston	TX	34
Columbia Univ. (NYP)	New York	NY	33
Abington Mem. Hosp. (UPenn)	Abington	PA	32

Sites with < 32 subjects enrolled: 161

Preparing A Detailed Event Narrative

It's a good idea to revisit the preparation of the outcome event narrative periodically throughout an event-driven study like POINT. We want our site investigators to write comprehensive, but concise, narrative descriptions of outcome events, primarily to assist our adjudicators. Consistent, unbiased interpretation of reported events is important to the quality, validity and credibility of POINT.

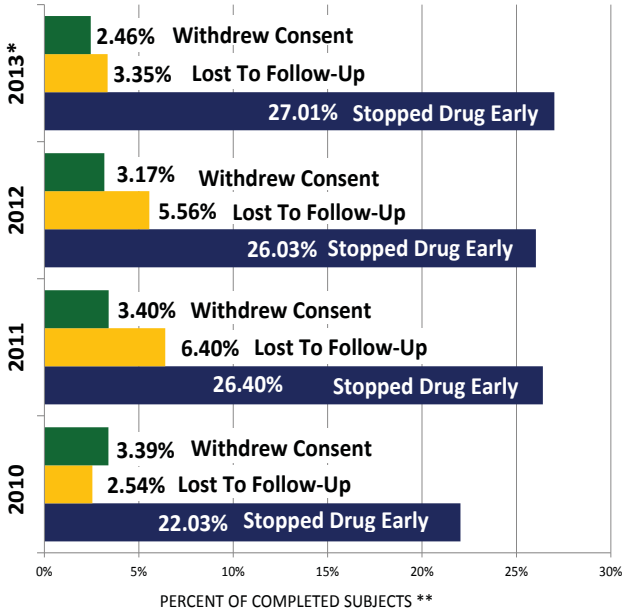
A well-written, comprehensive event narrative entered on Form 19: SAE/ Clinical Outcome Reporting Form should include the subject's age, race and gender, as well as a brief summary of the index event that qualified the subject for inclusion in the study. This can be followed by a description of the event, including what happened and all relevant clinical information. Summarize the subject's medical status prior to the event, signs and/or symptoms related to the event, differential diagnosis for the event, clinical course and treatment outcome.

Here are examples of the concise yet comprehensive narratives that we encourage sites to prepare, containing the information needed to guide POINT adjudicators when reviewing events:

A 63-year-old diabetic African American woman was enrolled in POINT after experiencing a right hemisphere minor stroke 15 days prior to this outcome event. Her carotid ultrasound study and ECG were normal. On the afternoon of admission, she was playing cards with friends when she suddenly experienced an intensely heavy and painful sensation in her mid-chest, along with shortness of breath. She was transported to a hospital where 30 minutes after its onset her chest pain persisted. An ECG showed prominent S-T segment elevation in leads II, III and AVF. Blood drawn 12 hours after symptom onset showed elevations of troponin. The subject received guideline recommended antithrombotic therapy and percutaneous coronary intervention (PCI) with placement of one bare-metal stent in the left main coronary artery. The interventionalist planned to discontinue her study drug and begin aspirin plus clopidogrel. Therefore, she requested unblinding of study drug treatment to determine if the subject should be loaded with clopidogrel. The subject did well over the next 2 days and was discharged to home.

An 82 year-old Caucasian male presented to hospital at 7:32 AM on 11-JUL-2012 with nausea, mild dizziness, and waxing and waning symptoms of left-sided weakness and numbness. His initial NIHSS was 6, and then improved to 3 after a CT scan and prior to enrollment. He was given ASA, enrolled in POINT and received the loading dose of study drug at 11:23 AM. He then had worsening left-sided weakness through the afternoon. A follow-up CT at 18:54 PM on 11-JUL-2012 excluded hemorrhage and the subject declined a recommended MRI study. His NIHSS was 9 on the morning of 12-JUL-2012 and symptoms remained stable on subsequent evaluations.

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 17, 2013

Q4 Site Activations

Box Hill Hospital, Box Hill, VIC, AUS (CRC); University of Calgary, Foothills Campus, Calgary, AB, CAN; Presbyterian Neurology Center, Charlotte, NC (CRC); **Enfant Jesus Hospital, QC, CAN (CRC); UPMC Shadyside Hospital, Pittsburgh, PA (UPitts);** Austin Hospital, Heidleberg, VIC, AUS (CRC); Charles LeMoyne, Greenfield Park, QC, CAN (CRC); Monash Medical Centre, Clayton, VIC, AUS (CRC); **Valley Baptist Med. Ctr., Harlingen, TX (Texas); John Hunter Hospital, New Lambton, NSW, AUS (CRC),** Palm Drive Hospital, Sebastopol, CA (CRC); London Health Sciences Center, London, ON, CAN (CRC); Huntington Memorial Hospital, Pasadena, CA (UCLA); **Providence Portland Med. Ctr., Portland, OR (CRC); Providence St. Vincent Med. Ctr., Portland, OR (CRC);** Abbott Northwestern Hospital, Minneapolis, MN (UMinn); Frederick Memorial Hospital, Frederick, MD (CRC); Gosford Hospital, Gosford, NSW, AUS (CRC); Vancouver General Hospital, Vancouver, BC, CAN (CRC); University Kansas Hospital, Kansas City, KS (UMinn); Grey Nuns Hospital, Edmonton, AB, CAN (CRC)

***Bold text indicates sites that have already enrolled subjects.**

Competing Trials

We have been informed that many POINT sites have been approached to participate in competing trials. One trial that is similar to POINT, but has a randomization window of 24 hours instead of POINT's 12 hour window, is SOCRATES. SOCRATES is sponsored by AstraZeneca, the manufacturer of ticagrelor, brand name Brilinta. Given the potential for recruitment overlap and/ or competition, AstraZeneca has agreed that patients that present within 12 hours of sympton onset should first be evaluated for enrollment in POINT at sites participating in both trials.

If you have any questions on dealing with competing trials at your site, please contact your Site Managers at the NETT and the CRC.

Biomarker Study Enrollment Tips

Here are some enrollment-boosting tips from the CRC:

- Add the Biomarker Study as an agenda item to monitoring review calls.
- Discuss obstacles to substudy enrollment on Study Coordinator calls.
- When a subject consents to participate in the substudy, send a follow-up email to the site to remind them of appropriate procedures, CRFs, and documentation.
- Send reminder emails to sites to include specific processes or requirements.

Please contact Trese Biagini, POINT Clinical Research Nurse, ***trese.biagini@ucsf.edu*** or (415) 502-7307 if you have any questions about the Biomarker Study.

International Stroke Conference 2014: San Diego, CA

POINT is hosting 2 events during the ISC on Wednesday, February 12, 2014 at the Hilton San Diego Gaslamp Quarter:

PI Reception for Site PIs and Coordinators:
5-7pm PST on the Outdoor Terrace

Advisory Committee Dinner Meeting:
7-9pm PST in the Marina AB Room

Please check your e-vites for these events.
For any ISC 2014 events questions, please contact:
Caitlin Glennon, Research Associate, UCSF:
caitlin.glennon@ucsf.edu or (415) 502-7309