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The Newsletter of the POINT Trial

Volume 4, Issue 4 4TH Quarter 2014

2014 4TH Quarter Recap

Dear Colleagues,

Happy New Year 2015!

Study Enrollment Update

We closed out 2014 with an enrollment of 2,522, including 74 subjects outside the US, reaching over 43 percent of our target of 5,840 subjects. The highest enrolling month in the quarter was December, with 63 enrollments. The fourth quarter also saw the first enrollments at one of our new Spanish sites. Thirteen sites were activated this quarter, including more sites in Canada as well as our first sites in the United Kingdom and Spain. Finland is up next! Welcome to all our new sites!

POINT ISC 2015: Nashville, TN

The UCSF POINT Clinical Coordinating Center will be hosting a reception for Principal Investigators and Study Coordinators during the International Stroke Conference (ISC) in Nashville, TN on February 11, 2015 at the Hilton Nashville Downtown (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.

Timing Of The Second Dose of Study Drug

This past November, we received an inquiry from a Study Coordinator regarding the timing of the second dose of study drug for a patient who received the loading dose at about 5am. Timing the second dose can be confusing, so we've added an FAQ to the POINT Toolbox on this topic for your reference (see FAQs 14 and 30).

December 2014 DSMB Meeting

We met with our Data and Safety Monitoring Board by teleconference on December 8, 2014 to review all interim data from the trial. The DSMB did not identify any concerns regarding safety or study implementation, and thus recommended the study proceed as planned.

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

Sincerely,

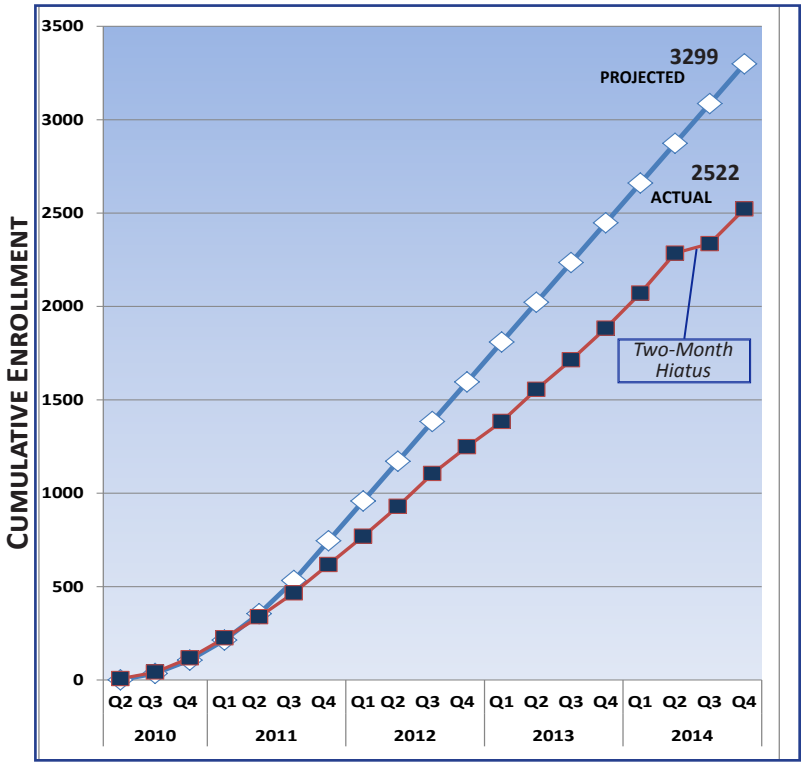
Clay Johnston MD, PhD, POINT Trial Principal Investigator

Don Easton MD, POINT Trial co-Principal Investigator

Anthony Kim MD, MS POINT Trial co-Principal Investigator

POINT Cumulative Enrollment

May 2010 through December 2014



POINT Enrollment Update: Total = 2522

Hot Enrollers for 4th Quarter

Place	Subjects	Site (Hub)
1	8	Guilford Neurological (CRC)
2	7	Desert Regional Medical Center (CRC), Santa Creu and Sant Pau Hospital (CRC)
3	6	Barnes Jewish Hospital (Cincinnati)
4	5	Northwestern University (CRC), University of Kentucky Hospital (Kentucky)
5	4	Buffalo General Medical Center (CRC), Froedtert Memorial Lutheran Hospital(Wisconsin), Providence Portland Medical Center (CRC), Shands Hospital At the University of Florida (CRC), Southern Illinois - Memorial Hospital (CRC)

Top Enrollers (as of December 31, 2014)

Site (Hub)	City	State	#
Guilford Neurologic (CRC)	Greensboro	NC	101
Hospital of UPenn (UPenn)	Philadelphia	PA	88
Benefis Hospitals Inc (CRC)	Great Falls	MT	47
Buffalo Gen. Hosp. (CRC)	Buffalo	NY	45
Columbia Univ. (NYP)	New York	NY	45
OHSU- Oregon (OHSU)	Portland	OR	44
Cleveland Clinic (CRC)	Cleveland	OH	43
Stanford Univ. (Stanford)	Stanford	CA	42
Detroit Receiving (Wayne)	Detroit	MI	41

COORDINATOR'S CORNER: ENROLLMENT AND RETENTION TIPS FROM THE CINCINNATI HUB (PART TWO)

This is the second part of last quarter's conversation with our Cincinnati Hub's Primary Study Coordinator, Irene Ewing. The Cincinnati Hub continues to be the NETT's top-enrolling hub this quarter, with 13 enrollments in the past 90 days. Keep up the good work, Cincinnati!

1) Is there routine discussion between staff members at any of your sites regarding patients who discontinue study drug early or terminate prematurely? Yes, we discuss each situation when it comes up. Our principal investigator follows up with a phone call to the patient and the primary care physician. We also discuss at our weekly stroke team meeting and at our monthly NETT meeting to determine whether there was anything we could have done differently during the time of enrollment or afterward to prevent this.

2) Is the staff at any of your sites trained on appropriate study subject retention methods? No one is officially trained, but all of our coordinators have years of experience with patient follow-up, so we know how to retain subjects. We gather as many names and phone numbers as possible. We get their address, place of employment, and primary care physician's contact information. We believe retention starts with the first encounter, so it is vital to develop a rapport with the patient and family from the beginning. They need to be invested in the trial.

3) What makes for a successful study team? At the site level: Communication is very important! Frequent re-training is also necessary. Discussions with the team regarding patient recruitment and retention issues (what went right and what went wrong) should be held on a regular basis. **At the Hub level:** You need to stay on top of the required regulatory documents, as well as communicate regularly with Spoke coordinators even if nothing is going on. There is a lot to track, so it helps if there is someone looking over things and reminding people. If one of my remote Spokes is late on something or has a data clarification request, I will send them a friendly email to let them know that. I think this helps them a great deal since they can be extremely busy. I also send them directions frequently. If you don't use WebDCU on a regular basis, it is easy to forget certain steps.

Study Drug Discontinuation: Reasons and Prevention Strategies

Study drug discontinuation continues to be a major problem. The rate of drug discontinuation amongst POINT subjects has steadily increased every year from 22.88% in 2010 to 30.75% in 2014 (see chart above).

As part of our presentation to the DSMB this past December, we provided a list of reasons for which patients enrolled in POINT choose to discontinue study drug. Below are some of the most common:

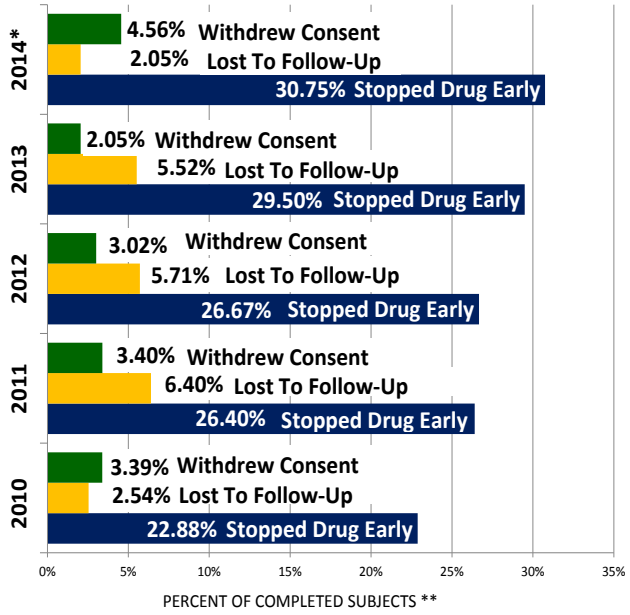
Reason for Study Drug Discontinuation	N	%
Experienced a possibly related adverse event (headache, GI, etc.)	138	21.7 %
Candidate for prohibited medication	138	21.7 %
Primary physician discontinued	104	16.4 %
Declined continuation after reconsideration	86	13.5 %
Total Discontinuing Study Drug Early	634	

Patients shouldn't be asked to continue taking study drug if they have a need for any prohibited medications (e.g., in the event of atrial fibrillation). However, the other three reasons for drug discontinuation listed above may benefit from more frequent communication between site staff, study subjects, and subjects' primary care physicians.

It is important that site staff maintain regular contact with subjects beyond the required follow-up visits. When study coordinators are aware of how their respective patients are feeling, it provides them the opportunity to address any concerns that may arise post-randomization.

Site staff should also do their best to engage subjects' primary care physicians. We give patients a letter explaining the study to present to their primary care physician at the follow-up visit. Study coordinators need to ensure that their patients' primary care physicians receive this letter by emailing/faxing it directly to them. For sites struggling with subject retention, it may be helpful for site principal investigators or co-principal investigators to call primary care physicians directly to explain the study.

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 19, 2014

Q4 Site Activations

Presence Saint Joseph Medical Center, Joliet, IL (CRC); Hospital del Mar, Barcelona, ESP (CRC); Sherbrooke University Hospital, Sherbrooke, QC, CAN (CRC); **Santa Creu and Sant Pau Hospital, Barcelona, ESP (CRC);** Royal United Hospital, Bath, Somerset, GBR (CRC); John Radcliffe Hospital, Oxford, GBR (CRC); **UPMC Northwest, Seneca, PA (UPitts); Renown Regional Medical Center, Reno, NV (UCSF); Chandler Regional Medical Center, Chandler, AZ (UAriz);** Mercy Health Saint Mary's, Grand Rapids, MI (CRC), Loma Linda University Medical Center, Loma Linda, CA (CRC); **Notre-Dame Hospital, Montreal, QC, CAN (CRC);** Royal Stoke University Hospital, Stoke-on-Trent, GBR (CRC)

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

International Stroke Conference 2015: Nashville, TN

POINT is hosting 2 events during the ISC on Wednesday, February 11, 2015 at the Hilton Nashville Downtown:

PI Reception for Site PIs and Coordinators: 5-7pm CST in the Bredesen Room

Advisory Committee Dinner Meeting: 7-9pm CST in Armstrong 2

Please check your e-vites for these events. For any ISC 2015 events questions, please contact: Karla Zurita, Research Analyst, UCSF: ***karla.zurita@ucsf.edu*** or (415) 514-5524