point–ers

The Newsletter of the POINT Trial

Volume 5, Issue 3 3rd Quarter 2015

2015 3rd Quarter Recap

Dear Colleagues,

SOCRATES and POINT: Overlapping Sites

As many of you know, enrollment in the SOCRATES Trial is expected to be completed by the end of October, 2015. Since many POINT sites also participate in SOCRATES, we would like to remind everyone of the key differences in the eligibility criteria of the two studies. This will be available on pocket cards as an easy reference for overlapping sites. Please refer to the table on page 2 for an easy comparison.

The end of enrollment in SOCRATES is an excellent opportunity to increase enrollment in POINT at sites where the two studies overlapped. The biggest challenge for overlapping sites may be the difference in the enrollment window. Remember, for POINT you must enroll participants **within 12 hours** of symptom onset.

Study Enrollment Update

International expansion in POINT continued in the second quarter, including our first activations in Mexico, France, and Germany. POINT is now active in 10 countries with 37 total international sites initiated. We ended the quarter with 3106 subjects, with a high of 67 subjects enrolled in August. We extend a warm welcome to all new sites, international and domestic!

February 2016 Enrollment Target

An enrollment restriction was placed on our funding for Year 5 by the NIH: 50% of the award was made available, with the remainder becoming available once a target of 3,500 enrollments has been reached.

We'd like to reach that target by the end of February 2016. We recognize this is a stretch target, but with the end of SOCRATES and the addition of new sites, we think we can reach the enrollment rate of 80 subjects a month that will allow us to achieve this goal.

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

Sincerely,

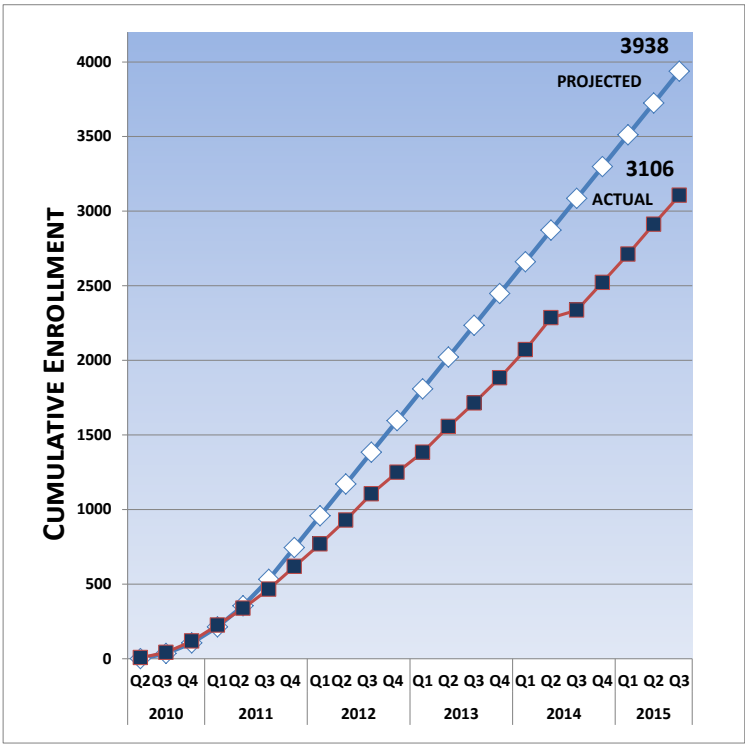
Clay Johnston MD, PhD, POINT Principal Investigator

Don Easton MD, POINT co-Principal Investigator

Anthony Kim MD, MS, POINT co-Principal Investigator

POINT Cumulative Enrollment

May 2010 through September 2015



POINT Enrollment Update: Total = 3106

Hot Enrollers for 3rd Quarter

Place	Subjects	Site (Hub)
1	9	Grady Memorial Hospital (Emory)
2	8	Miguel Servet Hospital (CRC)
3	7	Sinai-Grace Hospital (Wayne)
4	6	Santa Creu and Sant Pau Hospital (CRC), Northwick Park Hospital (CRC)
5	5	Cooper University Hospital (UPenn), Mayo Clinic Saint Marys Campus (Minn.), University of Kentucky Hospital (Kentucky)

Top Enrollers (as of September 30, 2015)

Site (Hub)	City	State	#
Guilford Neurologic (CRC)	Greensboro	NC	107
Hospital of UPenn (UPenn)	Philadelphia	PA	96
Benefis Hospitals (CRC)	Great Falls	MT	58
Buffalo General Med Ctr. (CRC)	Buffalo	NY	54
Stanford University (Stanford)	Stanford	CA	52
Columbia Univ. (NYP)	New York	NY	52
Detroit Receiving (Wayne)	Detroit	MI	49
Temple Univ. Hospital (Temple)	Philadelphia	PA	48
OHSU-Oregon (OHSU)	Portland	OR	48
Univ. of Kentucky (Kentucky)	Kentucky	KY	47
Memorial Hermann (Texas)	Houston	TX	46
Cleveland Clinic (CRC)	Cleveland	OH	45
Methodist Hospital (CRC)	Houston	TX	45
Abington Memorial (UPenn)	Abington	PA	45

Send your feedback and suggestions for future newsletters to Samantha.Applegate@ucsf.edu.

COORDINATOR'S CORNER: THE ROLE OF THE SUBJECT'S PCP IN MINIMIZING STUDY DRUG DISCONTINUATION

By Medina Sahak, Research Analyst (UCSF)

Premature study drug discontinuation continues to be a significant challenge in POINT: **over 25%** of subjects stop taking study drug while enrolled in the study. The POINT DSMB follows the rate of premature study drug discontinuation in the study closely, so we'd like to ensure we make every effort to minimize the number of subjects who come off study drug early.

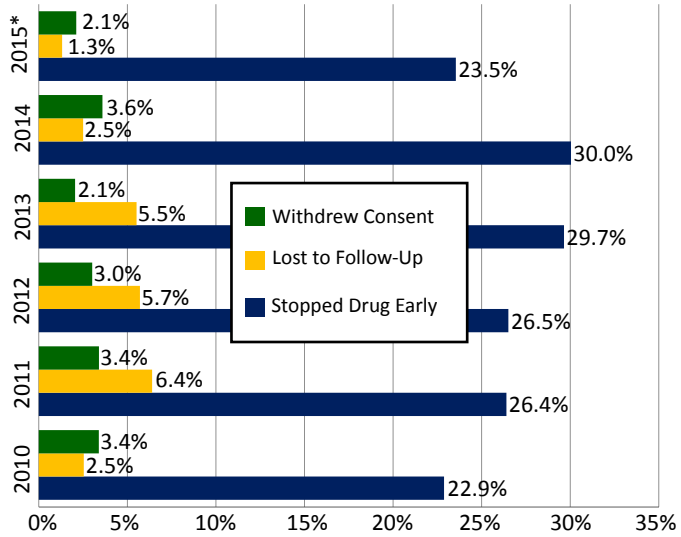
Therefore, after careful review of the data, we've divided the reasons for early study drug discontinuation into two categories: *unavoidable reasons* such as a subject's need for a prohibited medication, and *potentially avoidable reasons,* including discontinuation of study drug by the subject's primary care physician, or PCP. ***Early study drug discontinuation by the subject's PCP accounts for over one-third of the subjects coming off study drug before the full 90 days of treatment.***

The likelihood of reducing study drug discontinuation in POINT is greater for potentially avoidable reasons. The importance of the PCP in minimizing avoidable discontinuation of study drug represents an opportunity to refresh existing strategies and to develop and implement new "physician-facing" strategies. A key existing strategy is the PCP letter sent after a patient is randomized, available in the POINT Toolbox on the NETT website since the beginning of the study. The letter is intended to inform the subject's physician about the trial, and the importance of keeping a subject on the assigned intervention for the duration of participation in the study.

New outreach strategies such as "appreciation calls" are conducted with sites that have low rates of avoidable discontinuations, to allow those sites to share how they keep subjects on study drug for the full 90 days. A recent appreciation call with Santa Creu and Sant Pau Hospital in Barcelona, Spain (one of the top enrollers in POINT) allowed the local study team to share strategies on how to minimize premature study drug discontinuation. The team suggested that providing 24/7 coverage, using the WhatsApp group chat and engaging local neurologists not directly involved in POINT contribute to low rates of premature study drug discontinuation, as well as to high levels of recruitment.

We would be interested in hearing whether you think there are opportunities to use technology to maintain participants on study drug for the full 90 days of treatment. We are always open to new suggestions to help prevent subjects from coming off study drug early, so please feel free to forward your ideas to Medina Sahak (**medina.sahak@ucsf.edu**).

WITHDRAWN CONSENTS, LOSSES TO FOLLOW-UP, AND STOPPED DRUG EARLY



Percent of Completed Subjects**

*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 September 23, 2015

Top-Enrolling NETT Hubs (as of September 30, 2015)

Hub	*Total*	*Enrollments per 90 days*
UPenn	246	11.8
Wayne	141	6.9
Cincinnati	143	6.7
Minnesota	123	5.8

Q3 Site Activations

University Medical Center Leipzig, DEU (CRC); Foch Hospital, Suresnes, FRA (CRC); JFK Medical Center, Edison, NJ (CRC); Mexican Association for Clinical Research, Pachuca, HI, MEX (CRC); Cedars-Sinai Medical Center, Los Angeles, CA (CRC); **Good Samaritan Hospital, San Jose, CA (Stanford)**; Queen Elizabeth University Hospital, Glasgow, GBR (CRC); Vall d'Hebron Hospital, Barcelona, ESP (CRC); Burgos University Hospital, Burgos, ESP (CRC); Neurosciences Clinical Trials S.C., Culiacan, SI, MEX (CRC)

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

Biomarker Specimen Collection

Please remember to periodically check the collection dates on your Biomarker specimens. If you are using a -70°C to -90°C freezer, specimens must be shipped within **3 months** of the collection date. If you are using a -20°C, -30°C, or -40°C freezer, the specimens must be shipped within **4 days**.

POINT vs SOCRATES Eligibility Criteria

	POINT	SOCRATES
Qualifying Event: Minor Ischemic Stroke	Residual deficit with **NIHSS ≤ 3** at randomization	Residual deficit with **NIHSS ≤ 5** at randomization
Qualifying Event: High-risk TIA*	Complete resolution of deficit at randomization with ABCD2 score ≥ 4	Complete resolution of deficit at randomization with ABCD2 score ≥ 4
Randomization Window	Within **12 hours** of symptom onset	Within **24 hours** of symptom onset
Age	**18 years** of age or older	**40 years** of age or older
Other Studies of Investigational Therapy/Treatment	Participation within last **7 days** is an exclusion	Participation within last **30 days** is an exclusion

*Eligibility criteria are the same.