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The Newsletter of the POINT Trial

Volume 7, Issue 4 4th Quarter 2017

2017 4th Quarter Recap

Dear Colleagues,

Study Enrollment Update
As most of you know, the NINDS has discontinued new enrollment into the POINT Trial based on the recommendation of the Data and Safety Monitoring Board (DSMB), which met on December 18, 2017.

The DSMB and NINDS had no administrative concerns and indicated that follow-up of already randomized patients should continue per the study protocol.

New enrollment was discontinued at 4,890 subjects: 4,043 in the United States and 847 in countries outside of the United States. Follow-up of those already enrolled continues. Thank you for all your efforts over the past seven years.

We would like to recognize the Hub teams that enrolled more than 150 subjects into the POINT Trial. They are:

- Emmes (CRC sites in the US: 1,849)
- HCR/NTA (CRC sites outside the US: 847)
- UPenn (345)
- Cincinnati (209)
- Minnesota (196)
- Wayne (191)

Closeout FAQs and Open DCRs
We have compiled a list of FAQs regarding study closeout on page 2 of this newsletter. Any additional updates will be posted on the NETT Toolbox, particularly as we approach database lock, reporting, and publication.

As a reminder, please be sure to respond to data queries promptly and reconcile all overdue CRFs, overdue visits, and open rule violations. WebDCU™ will be contacting sites that have overdue items individually. Please contact Kavita Patel (pateka@musc.edu) for WebDCU data-related questions.

You may reach out to your Study Manager or CRA with questions about additional study closeout activities at your site.

POINT at the ESOC 2018: Gothenburg, Sweden
Please be on the lookout for information about the final POINT Investigator Meeting in the next several months. It will take place during the European Stroke Organization Conference in May 2018.

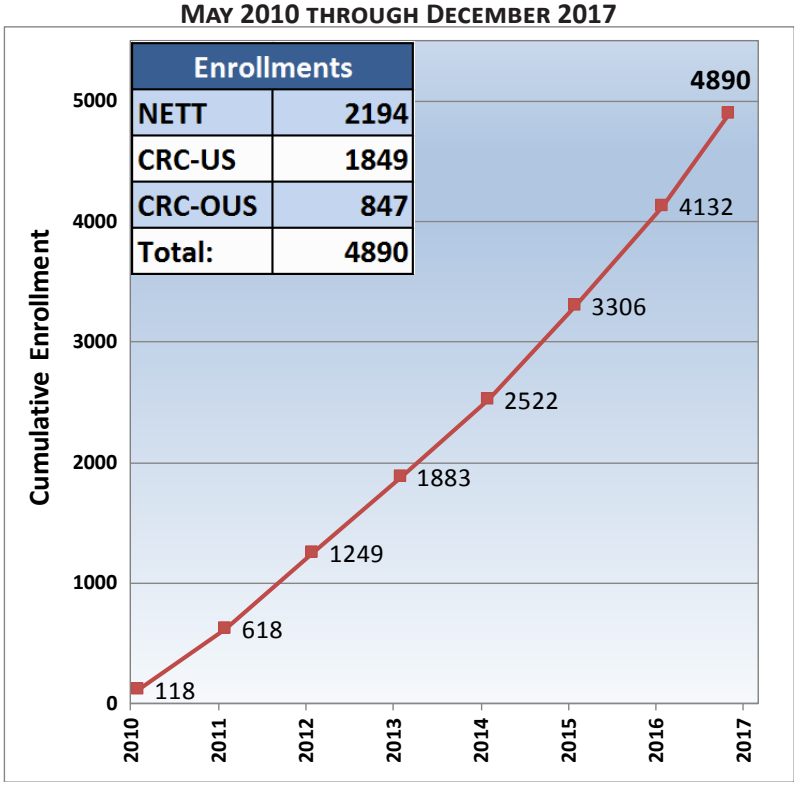
Thank you for your efforts in making POINT happen. We will be in touch.

Sincerely,
Clay Johnston MD, PhD, POINT Principal Investigator
Don Easton MD, POINT co-Principal Investigator
Anthony Kim MD, MAS, POINT co-Principal Investigator

In This Issue: *Closeout FAQs and Site-Level Closeout Activities*

POINT Cumulative Enrollment

May 2010 through December 2017



Hot Enrollers for the 4th Quarter

Hub	Site	#
CRC	Helsinki University Central Hospital, Helsinki, FIN	6
CRC	Hospital Donostia, Donostia, ESP	5
CRC	La Fe University Hospital, Valencia, ESP	5
CRC	Miguel Servet Hospital, Zaragoza, ESP	5
CRC	Pierre Wertheimer Hospital, Bron, FRA	5
CRC	University of Alberta Hospital, Edmonton, AB, CAN	5

Top Enrolling Sites in POINT

Hub	Site (US)	#
UPenn	Hospital of the University of Pennsylvania, Philadelphia, PA	126
EMMES	Guilford Neurological Associates, Greensboro, NC	124
EMMES	Benefis Hospitals Inc, Great Falls, MT	108
Stanford	Stanford University Medical Center, Stanford, CA	86
Emory	Grady Memorial Hospital, Atlanta, GA	77
NYP	NYP Columbia University Medical Center, New York, NY	71
OHSU	Oregon Health & Science University Hospital, Portland, OR	71
EMMES	Buffalo General Medical Center, Buffalo, NY	67

Hub	Site (Outside of the US)	#
CRC	University of Alberta Hospital, Edmonton, AB, CAN	109
CRC	Santa Creu and Sant Pau Hospital, Barcelona, ESP	76
CRC	University of Calgary - Foothills Campus, Calgary, AB, CAN	53
CRC	Foch Hospital, Suresnes, FRA	34
CRC	Helsinki University Central Hospital, Helsinki, FIN	34
CRC	Miguel Servet Hospital, Zaragoza, ESP	34
CRC	Vall d'Hebron Hospital, Barcelona, ESP	33
CRC	Girona University Hospital, Girona, ESP	30

CLOSEOUT FREQUENTLY ASKED QUESTIONS (FAQs)

Q. What should we tell subjects still in the study?

A. Tell them that new enrollment has stopped but the study and follow-up otherwise continues as planned.

Q. When will participants be told to which arm they were randomized?

A. This information will be provided to each site as soon as possible after the primary paper is published.

Q. Do subjects need to stop study drug?

A. Those subjects who have not completed the study should continue study drug and follow-up for the full 90-day follow-up period as planned.

Q. Are there any concerns with additional use of anticoagulants?

A. Anticoagulants have always been, and continue to be, prohibited concomitant medications in POINT.

Q. Do the findings increase the risk to subjects?

A. The answer is known to only the independent DSMB, the unblinded statisticians and the NINDS, but POINT has been assured that the study should continue, and that all subjects still on study drug should continue on it for the full 90-day follow-up period.

Q. Are there required changes to the consent documents?

A. Since all active subjects are already in the trial, and the DSMB and NINDS have recommended that they continue the study for their full 90 days, no changes to consent documents are necessary.

Q. When will the results be available?

A. Follow-up will continue for 90+14 days from the date enrollment ceased (i.e., Dec 18, 2017), and then some, as the close out process proceeds (late outcomes are reported, translations of source documents are completed for adjudication, data are cleaned, the database is locked, the primary publication is generated, etc.). This means several months from now.

It is expected the top line results will be provided to the investigators immediately prior to release of the published full results.

Q. Which publication will publish the results?

A. It is expected to be a top line journal, but is unknown at this time.

Q. When will the results be presented at a conference?

A. This is uncertain and will be until the likely date of the database lock becomes clearer. Our target is to present the results at the European Stroke Organization Conference in Gothenburg, Sweden, May 16-18, 2018.

Q. Why did it take so long for this (issue) to become apparent?

A. The DSMB monitored POINT for efficacy, safety and futility in the manner prescribed in the Study Protocol, and in the more detailed Statistical Analysis Plan which included formal stopping rules. The DSMB applied its judgment, based on regular assessments of the accumulating data. DSMB recommendations to stop a trial, stop enrollment but continue a trial, or other modifications, can occur at any time based on the observed data.

Q. Why wasn't the trial stopped sooner?

A. New enrollment has been stopped, but follow-up of already enrolled participants should continue. We must assume that the DSMB's assessment and judgment did not warrant an earlier intervention, as we all remain blinded.

Q. Was there a safety concern?

A. The DSMB has recommended that new enrollment be stopped, but that follow-up of already enrolled participants should continue. We will learn the reason for this recommendation after the trial results are published.

Q. Is it unusual to stop a trial so close to the end of enrollment?

A. Trials have been modified at every stage, and POINT still had 16% of its planned enrollment to complete.

Q. Can I get a copy of the meeting minutes?

A. The DSMB/NINDS provides only the letter referred to above. No minutes or reports are provided to the study team until the primary results are published.

The letter from NINDS, the Open DSMB Report for IRBs, version 6.0 of the Study Protocol and version 8.0 of the Statistical Analysis Plan are available in the POINT Toolbox on the NETT website: https://nett.umich.edu/clinical-trials/point/toolbox.

NETT, CRC, and OUS Closeout Procedures at the Site Level

As subjects end their participation in POINT, individual sites will be contacted by their Study Manager or CRA regarding local closeout activities. Site-level closeout activities will include, but are not limited to:

- A remote or in-person closeout visit
- Verification of consent procedures and documentation
- Verification of IRB communication of Study enrollment suspension
- Submission of all Adverse Events
- Destruction of remaining study drug

Please note that CRC sites should not destroy study drug until receiving an authorization memo from the CRC. Should there be any questions about study closeout, please reach out to the following contacts:

NETT Sites: Renee Kasperek-Wynn (kasperr@med.umich.edu)
CRC Sites (Emmes/OUS): Kimberly Vogan (kvogan@emmes.com) or Lahna Jones (ljones@emmes.com)