point–ers

The Newsletter of the POINT Trial

Volume 8, Issue 1 2nd Quarter 2018

2018 2nd Quarter Recap

Dear Colleagues,

Trial Results Presentation
As you already know, the results of the POINT Trial were presented at the European Stroke Organization Conference (ESOC) in Gothenburg, Sweden in mid-May.

The presentation room was packed with about 4,000 attendees, and the group broke into applause when the first results slide was presented.

The primary paper – *Clopidogrel and Aspirin in Acute Ischemic Stroke and High-Risk TIA* – is available through the New England Journal of Medicine (see link below).

Call for Proposals
The POINT Publications Policy is now available on the NETT Website under POINT (see link below). If you would like to submit a manuscript proposal for review by the POINT Executive Committee, please read the submission guidelines and complete Appendix A. The form can be submitted to mary.farrant2@ucsf.edu.

The full listing of secondary and tertiary analyses can be found on the reverse side. We will update you on the proposals for analysis of POINT data in future newsletters.

Links to Results and Manuscript Proposal Materials
Article on the New England Journal of Medicine Website:
NEJM.org >> Search: NEJMoa1800410

POINT Results Presentation Video and Slides for Site Teams at the ESOC:
NETT.UMich.edu >> POINT >> Results

ESOC Interview with Kennedy Lees and Clay Johnston:
YouTube.com >> Clinical Trials - POINT

Press Release: Dell Medical School - UT Austin
DellMed.utexas.edu >> Search: Stroke Prevention Drug Combo Shows Promise, Study Says

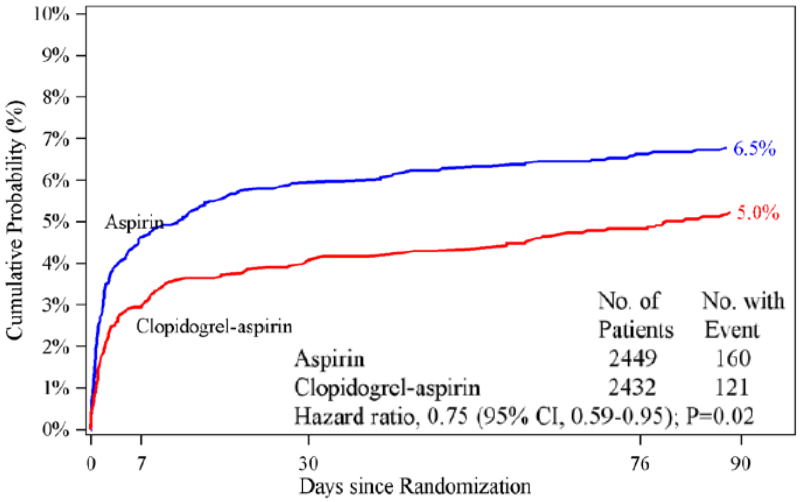
POINT Publications Policy and Appendix A
NETT.UMich.edu >> POINT >> Results

Thanks again for an incredible 8 years.

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: *Site-Level Closeout Activities* for NETT and CRC-US and OUS Sites

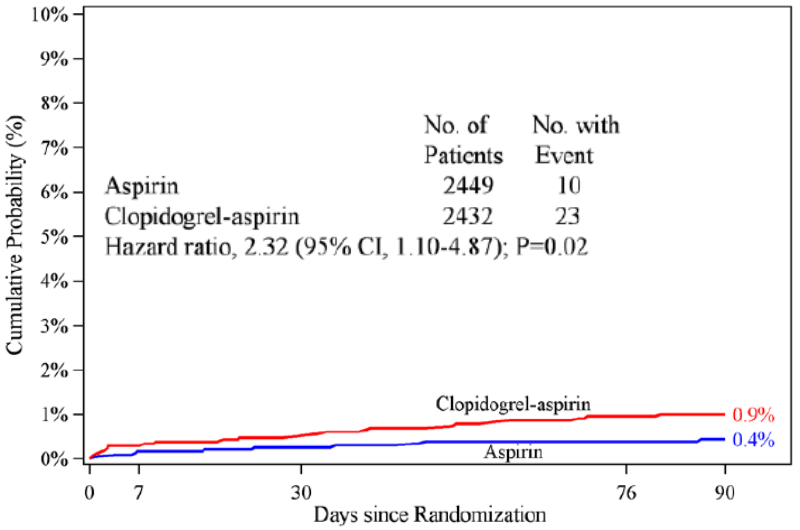
Primary Efficacy Outcome: Ischemic Stroke, Myocardial Infarction, or Ischemic Vascular Death



	Number at Risk				
Day	0	7	30	76	90
Aspirin	2449	2269	2153	2105	1365
Clopidogrel-Aspirin	2432	2279	2179	2113	1445

The composite primary efficacy outcome occurred in 121 patients (5.0%) receiving clopidogrel plus aspirin and in 160 patients (6.5%) receiving aspirin alone (hazard ratio, 0.75; 95% confidence interval [CI], 0.59 to 0.95; P=0.02)

Primary Safety Outcome Major Hemorrhage



	Number at Risk				
Day	0	7	30	76	90
Aspirin	2449	2372	2271	2230	1448
Clopidogrel-Aspirin	2432	2336	2257	2192	1505

The primary safety outcome of major hemorrhage occurred in 23 of 2432 patients (0.9%) receiving clopidogrel plus aspirin and in 10 of 2449 patients (0.4%) receiving aspirin alone (hazard ratio,2.32; 95% CI, 1.10 to 4.87; P=0.02)

REGULATORY CLOSEOUT AT NETT SITES

Message from Renee Kasperek-Wynn, RN, BSN

Thank you for addressing remaining items needed to close out your site. A document has been created for each site – *IRB Closeout Acknowledgement* – to upload the final IRB communication, acknowledging your site's permanent closure. The final step will be to submit the eDOA log to provide an end date for any remaining active staff. Please feel free to contact me at kasperr@med.umich.edu if you have questions.

Thank you,

Renee Kasperek-Wynn, RN, BSN

REGULATORY CLOSEOUT AT CRC-US AND CRC-OUS SITES

Message from the CRC Staff

Now that the POINT subject clinical database has been locked within WebDCU™, CRC staff will follow up with site staff at Emmes, Harrison, and NT Australia Hub sites regarding site regulatory and closeout items.

The CRC staff will contact site teams to schedule monitoring review calls and coordinate site closeout activities. For these closeout activities, a full review and accounting of site and staff regulatory documents will be completed. In addition, review of proper regulatory reporting for study subjects will be completed (i.e. SAE, protocol deviation reporting per IRB/EC/Regulatory Authority guidelines).

Site teams will be provided with POINT site closure documents to complete and CRC staff will follow up with site teams regarding closeout activities with the local or central study IRBs.

The regulatory module of WebDCU will remain open so outstanding regulatory items can be addressed prior to site closure.

For questions regarding the closeout process please contact CRC staff at crc@emmes.com, or your local CRA.

Thank you,

The CRC Staff

TRIAL RESULTS Q&A SESSION WITH POINT PI CLAY JOHNSTON

Please join us for a short presentation and a Question & Answer session with Clay Johnston on Wednesday, 27 June 2018, at 12pm ET (11am CT, 9am PT)

Web Portion:
https://connect.umms.med.umich.edu/nett_seminar/

Call-In:
888-330-1716 x 5967697

POINT SECONDARY AND TERTIARY ANALYSES

Secondary analyses will be performed to evaluate of the impact of therapy. ITT analyses and As-treated analyses will be performed for the following secondary outcomes for efficacy/net benefit:

- Composite event of ischemic stroke, MI, ischemic vascular death, or major hemorrhage
- Ischemic stroke
- Ischemic vascular death
- MI
- Composite event of ischemic stroke and hemorrhagic stroke

ITT analyses and As-treated analyses for efficacy/net benefit will be performed for the following secondary outcomes for safety/tolerability:

- Primary efficacy outcome from day 0 to 7 and day 8 to 90, and from day 0 to 30 and day
- 31 to 90 (HR and 95% CI will be calculated via cox model for each time point stratified)
- Primary safety outcome from day 0 to 7 and day 8 to 90, and from day 0 to 30 and day
- 31 to 90 (HR and 95% CI will be calculated via cox model for each time point stratified)
- All-cause death
- Hemorrhagic stroke
- Symptomatic intracerebral hemorrhage
- Other symptomatic intracranial hemorrhage (SAH, SDH or IVH)
- Major hemorrhage other than intracranial hemorrhage
- All minor hemorrhage (including asymptomatic intracranial hemorrhage)

Tertiary analyses (given sufficient number of events, >15 events in total for both treatment arms, are available for analyses to be meaningful):

- Composite of ischemic stroke, MI, all-cause death, or major hemorrhage
- Composite ischemic stroke, TIA, MI, or ischemic vascular death
- TIA (as outcome)
- Coronary revascularization
- Vascular death
- SAEs together and by major class (MedDRA Body System)
- New handicap/disability defined as 90 day mRS (>=2)
- 90 day mRS (ordinal)
- Asymptomatic intracranial hemorrhage (ICH, SAH, SDH or IVH)