Reviewer’s report

Title: The REstart or STop Antithrombotics Randomised Trial (RESTART) after stroke due to intracerebral haemorrhage: statistical analysis plan for a randomised controlled trial

Version: 0 Date: 09 Feb 2019

Reviewer: William Meurer

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TRLS 18-01070

This statistical analysis plan for the RESTART trial provides many details of the rigorous procedures used in this important study. The substance is all excellent (and of course, unlikely to change given the timing). I have a few suggestions that might strengthen this manuscript.

1. Reading this, it is a bit unclear at what time point most participants will be assessed. While this may be covered in the clinical paper - it would be helpful to add this detail here (briefly). Will it generally be during the acute hospitalization, rehab, or in the clinic afterwards?

2. On line 156, I think the word huge can be deleted. "Preserve fully the benefits of randomization" is less bombastic. Most readers of Trials are in favor of randomization.

3. I understand that this isn't classically non-inferiority or superiority. That said, you state you are attempting to estimate a "treatment effect." Since the primary outcome is recurrent ICH, and it is unlikely that the anti platelets will reduce the risk of ICH, I find this a bit confusing. It seems to me the point of this trial is to avoid recurrent thromboembolic events without increasing (substantially) hemorrhage events (mainly ICH). To me, it seems like the mRS analysis is really the most important one (although obviously more complicated) since this captures disabling ischemic and hemorrhagic stroke on the same scale (along with fatal hemorrhage and fatal non-brain thromboembolism like pulmonary embolism). If possible, perhaps expand the discussion so that the reader can better understand the goals. To me, it seems like the treatment effect is reducing disabling events (on the whole), yet the primary analysis is biased as ICH events should be more frequent in patients with anti-thrombotics. Again, I am just not certain if how to interpret your study if the time to recurrent ICH HR is 1.4 in the anti-thrombotic group, yet the mRS is better in that group. I am not expecting a change to you plan - but perhaps some additional context in the discussion would be helpful.

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