International **S**tudy of **C**omparative **H**ealth **E**ffectiveness with **M**edical and **I**nvasive **A**pproaches

Protocol Clarification Memorandum #2

July 22, 2014
for
ISCHEMIA Trial Protocol version 2.0, dated January 6, 2014

Summary of Clarification: The purpose of this memo is to clarify a detail in protocol Appendix A (Ischemia Test Eligibility Criteria) and report minor administrative discrepancies. This change will not have any effect on participant safety, the risk-to benefit ratio of study participation, or study informed consent forms.

Clarification

In Appendix A (Ischemia Test Eligibility Criteria) of the Protocol, criterion 4a of Exercise Test without Imaging is unclear in the Table entitled Criteria for at least Moderate Ischemia by Stress Test Modality.

Criterion 4a states:
Peak workload not to exceed completion of stage 2 of a standard Bruce protocol or ≤7 METS if a non-Bruce protocol is used

This Memorandum clarifies criterion 4a as follows:
Workload at which ST segment criteria are met is not to exceed completion of stage 2 of a standard Bruce protocol or 7 METS if a non-Bruce protocol is used

Discrepancies

Section 4. Study Design, Paragraph 1: Disregard the reference to Section 19.

Section 4.1. Study Flow, Paragraph 1, Sentence 1: Refer to **Appendix A** not Section 1.1 for more information about Criteria for at least Moderate ischemia by Stress Test Modality.

Figure 1, Footnote 3. Refer to **Section 5.5** and MOO not Section 6.5 for information about participants with eGFR≥60 who may not undergo CTA.

Section 9. Schedule of Assessments, Cath and Revascularization for participants randomized to INV strategy (protocol assigned); also applies to all revascularization procedures for participants in both management strategies, Fourth Bullet: 3rd sub-bullet that was in prior version of protocol and is included in Summary of Changes and current version of the schedule of assessments (Table 2) was inadvertently omitted – see below:

- For participants undergoing CABG
  - 12 lead ECG to be performed on day 3 post-CABG or at hospital discharge whichever comes earlier, and as needed for chest pain
  - All pre- and post-procedure operative biomarker measurements that are obtained should be recorded on eCRF
  - **Blood draw for both CK-MB and troponin before CABG and at 18±6 hours post CABG, whenever possible.**

All administrative corrections including grammatical corrections and clarifications will be incorporated into the next revision of the protocol.