



ACRIN PA 4005

*Randomized Controlled Study of a Rapid “Rule Out” Strategy
Using CT Coronary Angiogram Versus Traditional Care
for Low- to Intermediate-Risk ED Patients with Potential Acute Coronary Syndromes*

SUMMARY OF CHANGES

March 9, 2011

Amendment # 4 and Administrative Update

Besides routine revisions for style and grammar, Amendment 4 includes clarifications: to clarify that 30-day and 1-year follow-up contact with the participant should be initiated after 30 days and 1 year “from the triage/presentation date” as opposed “from randomization” (which may not occur until the following calendar day), to clarify when participants should be replaced because of confounding factors prior to diagnostic imaging—and which participants will still be followed for MACE even though diagnostic imaging may not have been performed, to allow for institutional standard-of-care practice in confirming negative pregnancy status among females of childbearing age, to advise sites to report total amount of contrast used and total radiation dose for each CT coronary angiography, and to allow for “up to” 3 blood samples to be collected within the University of Pennsylvania Health System (in case 3 samples cannot be collected at the recommended time points).

An Administrative Update was introduced to correct a typo in Group identification (the CCTA group was identified as “A” instead of “B” in Section 7.3) in Amendment 4.

Cover Page

Amendment 4 and version date March 9, 2011, have been added.

Administrative Update on March 25, 2011, has been added.

Table of Contents

Page numbers were adjusted to match the current version.

Schema, Page 3

Under “Group A: Traditional ‘Rule-Out’ Arm” and “Group B: CT Coronary Angiography ‘Rule-Out’ Arm”, 3rd and 4th bullets, respectively: Have been updated to allow for “up to” 3 serum collections for banking, in case the sites are unable to collect all 3 requested samples.

Under “Follow Up: 30 Days and 1 Year From Triage/Presentation Date”: Header has been revised to specify “From Triage/Presentation Date”.

Sections 3.2.4 and 3.2.5, Secondary Aims, Page 10

“randomization” has been corrected to “triage/presentation” in one location for each section.

Section 4.0, Study Overview, Page 11

2nd paragraph, 2nd sentence: Has been revised to clarify that follow-up telephone interviews should be conducted “after 30 days and after 1 year from triage/presentation”.

3rd paragraph, 2nd sentence: “up to” has been added in relation to the number of blood collection time points for serum banking within the University of Pennsylvania Health System.

Section 5.0, Participant Selection/Eligibility Criteria, Pages 11–12

2nd paragraph has been moved to appear below Section 5.2 on page 12 and has been revised to read: “Creatinine clearance and troponin will be measured at baseline during Phase I of Visit 1 (see Section

8.1.1); results received prior to diagnostic assessment may impact diagnostic testing and trial participation. If the participant is later found to have a low creatinine clearance and is known to be randomized to the CT coronary angiography Group A, they will be subsequently removed from the study and replaced. If an elevated troponin level is discovered after randomization but prior to CT coronary angiography or stress testing, the participant will be treated according to institutional standard of care and will remain in the study for the intent-to-treat analysis. If after randomization, but prior to CT coronary angiography or stress testing, the participant is discovered to have had CT coronary angiography or normal catheterization results within the year prior to presentation, then the participant will be treated according to institutional standard of care and will be included in the analysis for intent to treat."

Section 5.2, Exclusion Criteria, Page 11

Section 5.2.5: "known" has been added.

Section 6.4, Accrual Goals and Safety Monitoring, Page 13

2nd paragraph, 3rd sentence: Has been corrected from "ACRIN PA 4006" to "ACRIN PA 4005".

Section 7.3, Registration/Randomization Protocol, Page 15

1st paragraph, new-final sentence: Has been added to read—"If the participant is randomized to the CT coronary angiography Group B and, because of an elevated D-dimer, does not receive the CT coronary angiography (for example, they received a pulmonary embolism [PE]-protocol CT scan), the participant will be removed from the study and replaced."

Section 8.0, Study Procedures, Page 18

2nd paragraph, 2nd sentence: "up to" has been added to allow for fewer than 3 blood samples to be collected within the University of Pennsylvania Health System "..., whenever possible".

Section 8.1.1, Phase 1 of Visit 1, Page 18

2nd bullet, previous-5th sub-bullet: Has been deleted as the creatinine clearance is not part of the baseline medical history and physical examination. It now appears as the 3rd bullet.

2nd bullet, new-9th bullet: Pregnancy should be reviewed as part of the medical history and should be conducted "as required by the standard of care at each institution".

3rd bullet: Has been added as described above for creatinine clearance measure.

4th bullet: "up to" has been added in relation to the blood sample collection.

6th bullet: "initial" has been added to specify the timing of the TIMI Risk Score assessment.

8th bullet: Has been revised to describe that the randomization code will be assigned to each participant.

Section 8.1.2.1, Traditional Standard-of-Care "Rule Out" Arm (Group A), Pages 18–19

2nd bullet: "dictated by standard of care" has been added to allow for no diagnostic testing.

4th bullet: "up to" has been added in relation to the blood sample collection.

Section 8.1.2.2, CT Coronary Angiography "Rule Out" Arm, Page 19

1st bullet: "or not clinically indicated" has been added.

Former-2nd bullet: Has been deleted as it does not apply to the CCTA arm.

Now-2nd bullet: "creatinine" has been added.

Former-4th bullet: Has been deleted as pregnancy testing defers now to institutional standard-of-care practice.

Now-4th bullet: Has been added to advise sites to report total amount of contrast used and total radiation dose

Now-5th bullet: “up to” has been added in relation to the blood sample collection.

Section 8.2, Visit 2: Follow Up—After 30 Days From Triage/Presentation Date, Page 20

Header has been revised to specify that the 30-day timeline begins from the date the patient presents/goes through triage in the emergency department.

1st paragraph: Clarification throughout has been introduced to ensure the 30-day timeline begins from the date the patient presents/goes through triage in the emergency department.

1st paragraph, final sentence: Has been added to ensure clarity in deferring to the triage/presentation date instead of the randomization date in determining when the 30-day follow-up timeline begins.

Section 8.3, Visit 3: Follow Up—After 1 Year From Triage/Presentation Date, Pages 20–21

Header has been revised to specify that the 1-year timeline begins from the date the patient presents/goes through triage in the emergency department.

1st paragraph: Clarification throughout has been introduced to ensure the 1-year timeline begins from the date the patient presents/goes through triage in the emergency department as opposed to the date of enrollment.

1st paragraph, final sentence: Has been added to ensure clarity in deferring to the triage/presentation date instead of the randomization date in determining when the 1-year follow-up timeline begins.

Section 8.4, Participant Replacement Criteria, Pages 21–22

Header has been updated to describe “participant replacement” as opposed to “off-study” criteria.

1st and 2nd bullets: Have been revised to describe alternative diagnostic assessment than the study-related CT coronary angiography for participants with elevated creatinine clearance measures and suspected pulmonary embolisms (PEs) that result in the use of a PE-protocol CT scan instead of the CT coronary angiography.

New-3rd bullet: Describes the need to replace participants who withdraw from the trial prior to diagnostic testing.

New-2nd paragraph: Has been added to ensure follow-up continues for these replacement participants to assess for MACE, as follows—

“However, should a participant meet any of these replacement criteria, sites will still conduct follow-up procedures for MACE (after 30 days and after 1 year post-triage/presentation date) for these participants (unless they formally withdraw from the trial).”

Section 8.5, Study Procedures Table, Page 23

Has been revised to reflect revisions to pregnancy test procedures, description of follow up timeline initiation at triage/presentation, and follow-up criteria among replacement participants as described in detail above.

Section 9.1, CT Coronary Angiography, Page 24

1st paragraph, new-6th sentence: Has been added to require sites to submit the total amount of contrast used and total radiation dose for the CT coronary angiography.

Section 15.1, Study Design and Endpoints, Pages 33–34

Section 15.1.1.1, 1st sentence: “randomization” has been changed to “triage/presentation”.

Section 15.1.2.3, 1st sentence: “randomization” has been changed to “triage/presentation”.

Section 15.1.2.4, 1st sentence: “randomization” has been changed to “triage/presentation”.

Section 15.2, Specific Aims and Analysis Plans, Pages 34–35

Section 15.2.1, 2nd paragraph, 3rd sentence: “randomization” has been changed to “triage/presentation”.

Section 15.2.2.4, 1st paragraph, 1st sentence: “randomization” has been changed to “triage/presentation”.

Section 15.2.2.5, 1st paragraph, 1st sentence: “randomization” has been changed to “triage/presentation”.

Section 15.4, Power Consideration, Page 36

Section 15.4.1, 1st paragraph, 1st sentence: “the index admission” has been changed to “triage/presentation”.

Section 15.6, Trial Monitoring, Page 37

1st paragraph, 2nd sentence: “from randomization” has been changed to “post triage/presentation”.

2nd paragraph, 1st sentence: “the index visit” has been changed to “triage/presentation to the ED”.

Appendix I, Informed Consent Form Template, Pages 45–49

Has been revised on pages 45, 46, 48, and 49 (two places in the Study Chart), to correct the description for the 30-day and 1-year follow-up timeline to relate the timing to the person’s arrival to the emergency department.

Page 46, under “Medical procedures that are being done specifically because you are in this study ...”, 2nd bullet: Has been revised to reflect pregnancy testing according to the institution’s standard practice.

Page 47, under “For Group A (Standard Care)”, 2nd paragraph, 1st sentence: “up to” has been added in relation to the blood sample collection.

Page 48, under “For Group B (Standard Care + CT Scan)”, 3rd paragraph, 2nd sentence: “up to” replaces “about” in relation to the blood sample collection.

Page 49, Study Chart, Phase 2 – After Registration and Randomization: Group B, 3rd row, 2nd column, former-4th bullet: Has been deleted as pregnancy test will not be conducted prior to CT coronary angiography per trial protocol.

Appendix IV, Clinical Data Collection Criteria, Page 57

3rd paragraph, 4th sentence: Has been revised to correct the description for the 30-day and 1-year follow-up timeline to relate the timing to the person’s arrival to the emergency department.

Appendix V, Blood Processing/Banking Protocol, Page 59

1st paragraph, 4th sentence: Has been revised to describe “Up to” 3 blood samples that will be drawn from consenting participants.