

MUSC and Study-Wide Amendments

Indicates Amendment with new Protocol Version

Original Study Approval

Approved on 4/19/2016

Amendment 1

Approved on 5/5/2016

- Personnel change- Add Eden Gebre and Claire Cox

Amendment 2

Approved on 6/21/2016

- Personnel change- removed Lynne Becker
- Protocol v. 6/14/16: Updated based on the kick-off meeting changes
 - Updated site list
 - Added follow up visit windows
 - Updated drug duration and administration times
 - Updated consenting and randomization procedures
 - Updated recruitment procedures
 - Updated inclusion/exclusion procedures
 - Added information regarding non-English speaking patients
 - Added and schedule of events table
- Consent and Consent Site Template v. 6/9/16:
 - Updated study medication administration section
 - Format changes
 - Updated randomization risks
 - Updated Site template to match main consent
- Fact Sheet and Site Template v. 6/14/16
- Uploaded data collection instruments
- Uploaded patient contact letters from GSR

Amendment 3

Approved on 6/23/2016

- Uploaded HIPAA Site Template v. 3.16.16
- Made HIPAA upload optional in the central IRB tab

Amendment 4

Approved on 6/23/202016

- Combined Consent and HIPAA forms into one document. PEPPER Combined ICF-HIPAA v. 6/9/16

Amendment 5

Approved on 7/20/2016

- Personnel Change- Added Carol Lambourne
- Updated Consent Forms

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- Combined ICF-HIPAA v. 7/20/16
- Combined ICF-HIPAA Site Template v. 7/20/16
- ICF Site Template v. 7/20/16

Amendment 6

Approved on 7/26/2016

- Combined ICF-HIPAA Site Template v. 7/26/16 and ICF Site Template v. 7/26/16:
 - Updated to include MUSC IRB information
 - Updated “site name” in HIPAA section to say “LOCAL SITE NAME”

Amendment 7

Approved on 8/12/2016

- Protocol v. 8/12/16:
 - Increased first follow up window to 4 weeks
 - Increased randomization window
 - Removed specific committee board members
 - Removed Site Names
 - Corrected grammatical errors
 - Generalized the enrollment goals
- Consent Changes
 - ICF Site Template v. 8/12/16
 - Combined ICF-HIPAA Site Template v. 8/12/16
 - Combined ICF-HIPAA v. 8/12/16:
 - Generalized enrollment goals
 - Increased first follow up window to 4 weeks

Amendment 8

Approved on 9/22/2016

- Protocol v. 9/1/16
 - Updated randomization paragraph regarding when patients and surgeons are told about the randomization assignment
- Allowing for the consenting of Spanish-speaking patients

Amendment 9

Approved on 11/18/2016

- Protocol v. 11/16/16
 - Removed Michael Terrin from protocol
 - Fixed grammatical errors
 - Updated Schedule of Events chart
 - Removed Axio as randomization host and updated role.
 - Added GSR as randomization host
 - Changed day of surgery aspirin dose to 162 mg in the morning
 - Updated dosing times of rivaroxaban to match coumadin

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- Added bilateral joint surgery to exclusion criteria
- Updated Inclusion/Exclusion Criteria
- Consent Changes
 - ICF Site Template v. 11/16/16
 - Combined ICF-HIPAA Site Template v. 11/16/16
 - Combined ICF-HIPAA v. 11/16/16:
 - Clarified percentage of patients who have complications
 - Updated Aspirin dosing on day of surgery and thereafter
 - Updated Rivaroxaban administration
 - Added urine pregnancy test to procedures.
 - Included mail, and email in the follow-up language
 - Grammatical changes
 - Removed the option for patient to be randomized to 1 of the 3 drugs if there is a contraindication to two.
 - Update AXIO's role in HIPAA
 - Updated GSR's role in HIPAA
- HIPAA Site Template v. 11/16/16
 - Updated Axio's role
 - Updated GSR's role
- Ads/Study Recruitment Materials
 - Uploaded brochure
 - Uploaded Recruitment Study Design Diagram v. 3.0
 - Fact Sheet: Added PEPPER logo to all
 - Fact Sheet v. 3.0
 - Fact Sheet Site Template v. 3.0
 - Fact Sheet Site Template- SPANISH v. 3.0
- Surveys (all version 3.0):
 - Added logo to all
 - Reformatted baseline and follow up surveys
 - Separated Follow up surveys:
 - 1 Month
 - 3/6 Month

ENROLLMENT STARTED 12/2/2016

Amendment 10

Approved on 12/15/2016

- Protocol v. 12/14/16
 - Removed Coumadin 2nd dose administration time of 8pm

Amendment 11

Approved on 5/25/2017

- Personnel Changes: Removed Eden Gebre and added Kelly Krajeck
- Combined ICF-HIPAA v. 4/20/17
 - Added statement regarding Dr. Friedman and Janssen into MUSC consent form

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Amendment 12

Approved on 7/18/2017

- Personnel Change: Removed Jacob Drew
- Added new resume for Spanish Translator
- Protocol v. 7/19/17
 - Added ability to obtain written consent via telephone
 - Inability to take the randomized medication due to financial constraints or due to new information that effects the patient’s safety will not require a protocol deviation.
 - Patient withdrawals:
 - Patients only withdrawn if they specifically request it
 - Patients who switch medications (into another arm of the PEPPER trial) will still remain in the study
 - The surgeon will assign the patient to another arm of the trial If they are unable to take the randomized med.
 - Participants are withdrawn if they do not receive one of the 3 PEPPER approved treatment groups.
 - Updated randomization window: coordinators can randomize within 10 days of the originally scheduled surgery. If a surgery is postponed after randomization, a protocol deviation is not required.
 - Added cancer/active treatment contraindication to Aspirin group
 - Updated Rivaroxaban administration timing- removed “no later than 6pm on the evening of post op day 1. Added “approximately 24 hours after completion of the index operation.”
 - Removed specific pharmacy where medication can be dispensed
 - Updated Statistical Analysis Plan
- Combined ICF-HIPAA Site Template-SPANISH v. 11/16/16
 - Updating to match currently approved English version
- Surveys (all v. 4.0)
 - Removed GSR signature
 - Added “N/A” option to stairs questions
 - Added medication question to 1 month surveys

Amendment 13

Approved on 9/19/2017

- Protocol v. 8/7/17
 - GSR name change to STATIX
 - Added Hip resurfacing to inclusion
 - Removed Social media language
- Consent/HIPAA
 - HIPAA Site Template v. 7/25/17
 - GSR name change to statix
 - ICF Site Template v. 7/25/17
 Combined ICF-HIPAA Site Template v. 7/25/17
 Combined ICF-HIPAA Site Template- SPANISH v. 7/25/17
 Combined ICF-HIPAA v. 7/25/17
 - GSR name change to STATIX
 - Updated cost section to include copay range for rivaroxaban

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- Study Design Diagram v. 4.0
 - Removed GSR logo and added Statix logo
- 1 Month Follow Up Surveys v. 5.0
 - Updated last question regarding medication

Amendment 14

Approved on 11/28/2017

- Personnel Changes: Added Emma Ricciardone and Jennifer Vollmer
- Spanish Surveys
 - Baseline v. 4.0
 - 1 month v. 5.0
 - 3/6 month v. 4.0
- Patient Contact Form v. 3.0
 - Removed ID number
 - Added line for alternative contact

Amendment 15

Approved on 2/13/2018

- Patient recruitment video script

Amendment 16

Approved on 7/19/2018

- Personnel: Adding Katie Kirchoff and Tomoko Goddard
- Uploading physician "business card" for sites randomizing to all 3 drugs as well as 2 drugs only.
- Protocol Version 7.16.18
 - Stratified randomization
 - Inclusion/Exclusion- added inclusion #4 "patient is eligible for randomization to at least two of the study anticoagulation regimens. Removed exclusion #4 "patients who have a contraindication to two or more of the three study prophylaxis regimens"
 - AE monitoring: coordinators responsible for ad hoc reporting as well as follow up on those patients who fail to respond to 6 month follow up attempts.
 - Randomization window: updated from "no earlier than 10 days before,..." to "after the surgeon confirms eligibility and up until the day before the originally scheduled surgery date."
- Consent Templates: added additional templates for those sites using restricted randomization
- Fact Sheet Templates: added additional templates for those sites using restricted randomization
- Study Design Diagram: added additional versions for those sites using restricted randomization
- Survey Updates:
 - Page numbers to all surveys
 - Updated medication questions to 1 month survey (patient's last dose/medication switching)

Amendment 17

Approved on 8/6/2018

- Added abbreviated survey for 6 month follow up attempts by coordinators.

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Amendment 18

Approved on 10/2/2018

- Personnel: added Kathy Weatherford

Amendment 19

Withdrawn

Amendment 20

Approved on 2/8/2019

- Surveys: added in 3 additional questions related to AEs on the follow up surveys

Amendment 21

Approved on 2/14/2019

- Surveys: added in 3 additional questions related to AEs on the Abbreviated follow up surveys

Amendment 22

Approved on 4/16/2019

- Personnel: Removed Kelly Krajeck; Added Lauren Card

Amendment 23

Approved on 5/21/2019

- Updated Randomization scheme from 2:1 to 1:1:
 - At PCORI's request, an external consultation and review was conducted of our proposed revised analysis plan that included a 2:1 randomization scheme at those sites restricted to either aspirin and rivaroxaban, or aspirin and warfarin. After consideration of this feedback and the potential confounders introduced by such a scheme, PEPPER's Data Coordinating Center, in consultation with Dr. Pellegrini and the PEPPER statistician team, intend to pursue a 1:1, i.e. balanced, randomization assignment at the subset of sites restricted to two medications. Moreover, the data analysis plan has been modified to reduce risk of confounding by site such that comparisons between drugs will only include patients from sites that could have randomized patients to either of the two drugs being compared. For example, the rivaroxaban-aspirin comparison will not include any aspirin patients from sites restricted to randomization to only aspirin or warfarin. Statistical power has been recalculated under these conditions and no meaningful detrimental effects are evident. PCORI have approved this change.

Amendment 24

Approved on 1/28/2020

- Update PEPPER Brochure to include Dartmouth-Hitchcock

Amendment 25

Approved on 4/21/2020

- Personnel: Removed Claire Cox; Added Jennifer Bean

Amendment 26

Approved on 4/30/2020

- Personnel: Add Hannah Stark as MUSC coordinator
- Updated UDAK number for new grant

MUSC and Study-Wide Amendments

Amendment 27

Approved on 6/10/2020

- Protocol Update v. 5.28.20
 - Removed AXIO, added CTRIC
 - Updated site enrollment goals
 - Added E-consent protocol
 - Added COVID-19 Sub Study information
- Consent Update v. 5.22.20 (all templates—MUSC, site, restricted randomization)
 - Removed AXIO
 - Updated site enrollment goals
 - Added E-consent line on signature page
 - Added Future Research option
- CRF Updates:
 - Patient Contact Form v. 5.0
 - Baseline (Hip and Knee) versions 8.0
 - 1 Month Follow Up (Hip and Knee) versions 9.0
 - 3/6 Month Follow Up (Hip and Knee) versions 9.0

Amendment 28

Approved on 1/13/2021

- Personnel: Add Dr. Erik Hansen as participating MUSC surgeon

Amendment 29

Approved on 5/24/2021

- Personnel: Remove Hannah Stark as MUSC coordinator and add Ebony Panaccione

Amendment 30

Approved on 9/28/2021

- Added COVID-19 vaccination questions to baseline and all follow-up surveys

Amendment 31

Approved on 1/7/2022

- Personnel: Remove Jenifer Bean, Tomoko Goddard, Katie Kirchoff, Emma Ricciardone. Add Emily Stitt

Amendment 32

Approved on 2/2/2022

- Personnel: Add Laura Kernan

Amendment 33

Approved on 7/28/2022

- Protocol Update v. 7.26.2022
 - Added NDI language on page 16

Amendment 34

Approved on 10/7/2022

- Updated Participant Business Cards v. 3.0
- Add Primary Care Physician Letter v. 9.27.22

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Amendment 35

Approved on 1/25/2023

- Personnel: Add Emma McLeod

Amendment 36

Withdrawn

Amendment 37

Approved on 5/2/2023

- Personnel: Add Dr. Voss

Amendment 38

Approved on 6/15/2023

- Protocol Update v. 6/14/2023
 - PCORI has approved the removal of the warfarin group for all future patients.
 - The milestones were updated where needed
 - Sample size was updated to approximately 20,000
 - The analysis plan has been updated to reflect the removal of warfarin at this stage in the trial.
- Consent Updates
 - Combined ICF/HIPAA Site Template v. 06.14.2023 (R.A.)
 - Updated sample size to approximately 20,000
 - Updated language in summary
 - Updated randomization language
 - PEPPER ICF Site Template v. 06.14.2023 (R.A.)
 - Updated sample size to approximately 20,000
 - Updated language in summary
 - Updated randomization language
 - All other versions (W.A) and 3 drug versions are obsolete
- HIPAA Updates
 - PEPPER HIPAA Site Template v. 06.14.2023 (R.A.)
 - Added information about using aspirin and rivaroxaban only
- Fact Sheet Updates
 - PEPPER Fact Sheet Site Template- V. 3.0- R.A.is the only applicable version. All other versions of the Fact Sheet are now obsolete

Amendment 39

Approved on 1/16/2024

- Protocol Update v. 1/11/2024
 - Updated to reflect changes to study timeline and milestones as requested by PCORI

Amendment 40

Approved on 2/9/2024

- Protocol Update v. 1/11/2024
 - Updated to include "4" that was missing from date on first page

Amendment 41

Approved on 2/13/2024

- Personnel: Add Zion Porter as additional MUSC coordinator

MUSC and Study-Wide Amendments

Amendment 42

Approved on 3/14/2024

- Personnel: Add Adina Harri