**AAST Multicenter prospective observational study of trauma patients on novel oral anticoagulants: Part B**

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**Significance**

Trauma remains the 5th leading cause of death in the United States, and the 9th leading cause of death among persons >65years old1. The number of elderly patients and those taking anticoagulants presenting to trauma centers have been increasing.2 Patients on Warfarin have been found to have worsened outcomes following injury, particularly in those with traumatic brain injury2,3. However, the effect of newer anticoagulants such as Dabagatran or Rivaroxaban on the outcomes of trauma patients is unknown. Already several case reports have emerged describing significant bleeding associated with the use of these novel agents.4-6 There is significant evidence to suggest that rapid recognition and reversal of anti-coagulation in patients with traumatic brain injury can decrease progression of intracranial hemorrhage and improve mortality.2,3 New drug specific reversal agents for the novel oral anticoagulants are now becoming available (see Table 1 below), however there is little data delineating their efficacy and impact on outcomes following trauma.

The overall objective of this study is to identify the injury patterns and outcomes among patients taking novel oral anticoagulants who did and those who did not receive drug specific reversal agents.

**Hypothesis**

We hypothesize that patients taking novel oral anticoagulants who are reversed with drug specific agents will have improved outcomes following trauma compared to patients not receiving reversal or those reversed with transfusion and prothrombin complex administration.

**Specific aims**

1. Document effect of drug specific reversal agents on outcomes following injury in patients on novel oral anticoagulants including progression of traumatic brain injury, bleeding requiring surgery, angiography, or other intervention, re-bleeding following intervention, and death.

3. Describe the variations between centers in the management and reversal of oral anticoagulants in trauma patients.

**Study design**

Prospective multi-center observational study of patients on novel oral anticoagulants admitted to Level 1, 2 or 3 Trauma Centers. Data and outcomes will be observational and involve no proscribed therapeutic interventions or alterations from standard patient care. Institutions and providers will conduct normal diagnosis and management procedures without interference from this study.

*Inclusion Criteria:* The following criteria must be met for patients to be eligible for this study:

1. All patients consulted on or admitted by the trauma service, including inter-facility transfers will be eligible for inclusion.
2. Currently on Dabagatran, Rivaroxaban, **Apixaban or other oral thrombin inhibitor or Xa** inhibitor

*Exclusion Criteria*

1) Prisoners or inmate status

2) Patients <18years of age

4) Pregnancy

*Data collected will include:*

1) Demographics such as age, gender, race\*

2) Injuries and injury severity\*

3) Initial assessment and management such as laboratory values of coagulation including TEG, CT findings, need for surgery/angiography, transfusion of blood products\*

4) Outcomes such as bleeding, re-bleeding and death\*

\*See data collection sheet

Enrollment need not be limited to centers with TEG/ROTEM capabilities, but if they are in use as part of the centers routine trauma protocols we would appreciate the collection of this additional information. We will plan to specifically invite centers who do use TEG/ROTEM as part of their trauma protocols and our goal is to have a goal of 50% of centers be TEG/ROTEM uses.

*Patient consent*

This is an observational study that will not alter institutional management protocols or patient care, as such enrollment in this study will pose no additional medical risk to participants. Thus, waiver of informed consent is requested. Data will be recorded on a data sheet and transferred to a secured database that is devoid of patient identifiers thus posing minimal risk of breach of confidentiality.

*Data entry and Analysis*

All data will be collected through the AAST MIT online data entry system.

*Timeline*

This study will be completed over a ­­­­30 month period

1) Recruitment of centers and IRB approval 4 months

2) Enrollment of patients 24 months

3) Data analysis and manuscript preparation 2 months

*Power calculations*

The rate of intracranial hemorrhage among the patients in the previous NOA study was 30% progression of ICH occurred in 17%; to detect a 50% decrease in progression of ICH due to utilization of drug specific reversal agents we would require 241 patients per group to achieve a 95% confidence interval at 80% power.

Mortality for patients in the current study was 7%, to detect a 2-fold decrease in mortality we would need 637 patients per arm to achieve a 95% confidence interval at 80% power.

Sixteen centers in the current study enrolled 213 patients on NOA’s during the 24 month data collection period. Assuming the incidence of patients on NOA’s remains steady we anticipate that with the participation of the current centers we will be able to enroll enough patients on NOA’s to detect a significant decrease in ICH progression and overall mortality in 6 years. We anticipate recruiting an additional 10-12 centers allowing us to close enrollment in 24-36 months.

**Table 1.**

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| --- | --- | --- |
| **Anticoagulants** | **Mechanism** | **FDA approved** |
| **Dabigatran (Pradaxa)** | Direct thrombin inhibitor | 2010 |
| **Rivaroxaban (Xarelto)** | Xa-inhibitor | 2011 |
| **Apixaban (Eliquis)** | Xa-inhibitor | 2012 |
| **Edoxaban (Savaysa)** | Xa-inhibitor | 2015 |
| **Reversal agents** |  |  |
| **Idarucizumab (Praxbind)** | Monoclonal antibody for dabigatran reversal | 2015 |
| **Andexanet** | Modified factor Xa for Xa-inhibitor reversal | In development- anticipated 2016 |

**References**

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