Usage of Praxbind® (idarucizumab) for Reversal of Pradaxa® (dabigatran) in the Indiana University Health System

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BACKGROUND

- Dabigatran is a direct oral anticoagulant (DOAC), specifically a direct thrombin inhibitor.
  - Food and Drug Administration (FDA) approved for both prevention and treatment of pulmonary embolism (PE) and deep vein thrombosis (DVT), prophylaxis for hip replacement surgery, or non-valvular atrial fibrillation (AFib).[1]
- Idarucizumab is a monoclonal antibody that selectively binds to dabigatran.[2]
  - FDA approved in October 2015 with the indications of urgent reversal of dabigatran for emergent surgery and life-threatening or uncontrolled bleeding.[3]
  - Idarucizumab immediately and completely reverses dabigatran's effects.[2]
  - The FDA accelerated idarucizumab's approval based on results from 283 patients.[4]
  - Continued approval of idarucizumab is contingent on an ongoing open-label trial.

METHODS

Study Objective: Evaluate the safety, efficacy, and appropriateness of idarucizumab use in a large hospital system.

- The study was a retrospective chart review of all patients that received idarucizumab within the Indiana University (IU) Health system.
- Each idarucizumab order from December 2015 until October 2016 recorded in the IU Health medical record was included.
- Patient demographics and clinical data were assessed to determine the appropriateness of idarucizumab's usage at IU Health.
  - Indication for idarucizumab administration.
  - Setting idarucizumab was administered
    - Hospital or emergency department (ED).
  - Anticoagulant initiated after idarucizumab usage.
  - Time post-anticoagulant initiated after idarucizumab administered.
- Secondary outcomes
  - Bleeding or thromboembolic events associated with idarucizumab use.

REFERENCES

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RESULTS

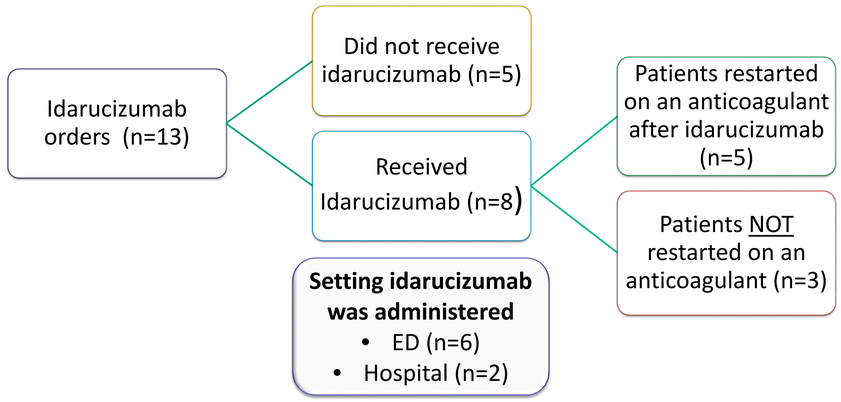

Table 1: Patient Characteristics

Characteristic	Results	Range
Age in years, mean	77.6	69-84
Males, n (%)	6 (75%)	
Indication for dabigatran		
AFib, n (%)	8 (100%)	

Surgeries or urgent procedures requiring idarucizumab

- Laparotomy for perforated bleeding duodenal ulcer (n=1)
- Surgery for small bowel obstruction (n=1)
- Laparoscopic cholecystectomy (n=1)

Life-threatening or uncontrolled bleeding requiring idarucizumab

- Bleeding duodenal ulcer (n=1)
- Hemorrhagic cerebrovascular accident (n=1)
- Upper gastrointestinal bleed (n=1)
- Stab wound (n=1)
- Esophageal cancer causing gastrointestinal bleed (n=1)

Reasons idarucizumab withheld (n=5)

- Bleeding controlled when factor VII and/or factor IX administered (n=2)
- Ordered on standby for pericardiocentesis surgery, but not given (n=1)
- Patient was not taking dabigatran initially (n=1)
- Patient discontinued dabigatran 3 months prior (n=1)

Safety

No bleeding or thromboembolic events occurred after idarucizumab.

Reinitiating anticoagulation after idarucizumab

Anticoagulant used

- Dabigatran (n=4)
- Enoxaparin (n=1)
- None (n=3)

Mean reinitiation time: 46 hours
Range: 27 – 264 hours

Outcomes when anticoagulant NOT restarted

- Hospital readmission for a blood clot 6 days later (n=1)
- Placed on mechanical thromboprophylaxis (n=1)
- Daily aspirin prescribed (n=1)

DISCUSSION

- **Current literature**
  - Anticoagulation experts from the Anticoagulation Education Task Force (AETF) have outlined scenarios where idarucizumab should and should not be used.[5]
    - These recommendations are summarized in Table 2.

Table 2: Appropriateness of Idarucizumab per AETF[5]

Recommendation	Clinical Scenario
Definite need for dabigatran reversal	• Life-threatening bleed • Bleeding in a closed space or critical organ • Persistent major bleed despite local hemostatic measures • Risk of recurrent bleeding due to delayed DOAC clearance or overdose • Patients at high risk for bleeding during emergency surgery or intervention
Reversal agent not generally recommended	• Elective surgery • Gastrointestinal bleeds that respond to supportive therapy • Drug overdose or accumulation without bleeding • Surgery that can be delayed to allow drug clearance

- **Prescribing idarucizumab**
  - Physicians in this study appropriately determined which patients needed and did not require idarucizumab for dabigatran reversal.
  - Idarucizumab was administered appropriately in 100% of recipients based on FDA indications.
  - When idarucizumab was withheld, it was because it was not an FDA approved indication.
  - There are currently no comparable studies that evaluate whether physicians are choosing appropriate candidates for idarucizumab.
  - This study demonstrates the usefulness of universal order sets and algorithms for the reversal of anticoagulants, which is also recommended by AETF.[5]
- **Safety**
  - There were no incidences of hemorrhagic events, thromboembolic events, or stroke within 24 hours in the 8 idarucizumab recipients.
- **Reinitiating an anticoagulant**
  - Anticoagulation reinitiation varied after idarucizumab administration.
  - The current guidance from the idarucizumab package insert states dabigatran may be restarted 24 hours after idarucizumab administration.[2]
  - In this study, the median time to restart an anticoagulant was 46 hours and ranged from 27 to 264 hours.
  - 37.5% of idarucizumab recipients never reinitiated an anticoagulant.
  - Future larger studies are recommended to determine when it is safe to restart an anticoagulant after idarucizumab.