Edoxaban effects on bleeding following punch biopsy and reversal by a 4-factor PCC: What we know, and what we know now.

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## Disclosures for Jerrold H Levy, MD, FAHA, FCCM

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<th>Research Support/P.I.</th>
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Presentation includes discussion of the following off-label use of a drug or medical device: Yes
Why is reversal important?

• Increases the safety margin of pharmacotherapy
• Facilitates management of critically ill patients or procedural intervention
• Provides new management strategies for patient care, bridging, and new paradigms
Anticoagulation Reversal Agents

- Inorganic molecules that bind to agent: PER977
- Biologic molecules that are decoys and competitively bind: Andexanet alfa
- Biologic molecules that non specifically bind as polyionic/polycationic interactions: protamine, rPF4
- MoAbs made to specifically bind to Rx: Idarucizumab for dabigatran
- Repleting biologic coagulation proteins: PCCs, rFVIIa
Correlation of INR With Factor Levels

Mean Factor Activity Levels vs INR

Adapted with permission from Gulati G et al. Arch Pathol Lab Med. 2011;135:
Edoxaban reversal with PCC: what does this study add?

• Although 2 previous studies show PCCs reverse rivaroxaban’s effect on PT/restore thrombin generation, this study is one of the first to show it reverses bleeding, in vivo-and is in agreement with animal studies.

• There is a lack of correlation between reversing laboratory tests and bleeding; extrapolating animal models and human volunteer data to bleeding patients should be cautiously interpreted as clinical bleeding is multifactorial.
However, this study supports the concept that PCCs should be considered as part of a multimodal approach to emergency reversal of Xa NOACs along with hemodynamic and hemostatic resuscitation for life threatening or other urgent bleeding episodes.
Summary

- PCCs reverse Xa inhibitors both in vitro and in anticoagulated volunteers; this is important bleeding data based on in vivo responses.
- More human data/studies are needed
- Additional novel therapies are in clinical trials that will provide new therapeutic strategies
- Therapy for NOAC bleeding should be multimodal
NOACs, DOACs, TSOACs: antidotes, anecdotes, and management strategies
Chinese Character of Blood

Blood Drainage after Surgery