Updated Results of the RE-VERSE AD Study

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Trial Design

**Strengths:**
1. Broad entry criteria facilitated enrollment of heterogeneous population
2. Two cohorts: bleeding and non-bleeding requiring emergency surgery or procedure
   
   Results generalizable to clinical practice

**Limitations:**
1. Open label cohort study
2. Hemostasis not rigorously defined - determined by local investigator
   
   Cautious interpretation of clinical outcomes
Results

Conclusive:
• Very effective – immediate, complete and sustained reversal of dabigatran as assessed by coagulation parameters.
• Safe – no prothrombotic, immunologic, or off-target concerns identified.

Reassuring but not definitive:
• Cessation of bleeding of 3.5 - 4.5 hours in Group A and “normal” intraoperative hemostasis in 93% in Group B must be interpreted cautiously given lack of placebo control and reliance solely on investigator assessment.

Sobering:
• Substantial mortality of ~19% at 90 days – removing the anticoagulant does not address vessel integrity or coexisting medical conditions.
Implications for Clinical Practice

1. Idarucizumab is remarkably effective in reversing the anticoagulation effect of dabigatran and has a clean safety profile: *first line in the management of patients taking dabigatran presenting with life-threatening emergencies.*

2. Simplicity in administration attractive: Ready-mixed solution and fixed dose of 5 grams IV for all patients. Rare (1.4%) need for second dose for rebleeding [can check for re-elevation of clotting factors].

3. Preventing bleeding likely has far greater impact than reversal - even with an “antidote”.

4. Serious bleeding with dabigatran [all NOACs] is rare – biggest impact of specific reversal agents may be reassurance.

5. Managing bleeding must incorporate early assessment for restarting anticoagulation: impressive efforts in RE-VERSE AD to have early re-initiation of anticoagulation led to low rates of thrombotic events.