

**NOAC Reversal Agents:
Defining the Data Elements for Safety and
Effectiveness Post-Approval**

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- 85 y/o WM
- A-fib, spinal stenosis, myasthenia gravis, history of falls
- On warfarin, some INR variability, several minor/moderate bleeds; considered NOACs
- Nov 2012-car broadsided, head contusions, small subdural

NOACs and Reversal Agents: General Comments

- NOACs: significant clinical innovations; create more options, potential to reduce underuse of effective treatment
- Gaps in evidence:
 - Real world evidence re NOACs (effectiveness, safety, patient clinical profiles)
 - Management of bleeding episodes in real-world clinical settings
- Likely high levels of variation in current and future practice re NOACs/bleeding:
 - Low incidence rates/site
 - Lack of clarity around definition(s) of “major” or “life threatening” bleeding
 - Variation in clinical presentation
 - Variation in treatment approaches-no standard protocol?
- Impact of Reversal Agent approval-Could be mixed
 - Could increase appropriate use of NOACs and create net increased clinical benefit
 - Could increase inappropriate use or create net decreased clinical benefits (“Behavioral offset”; change in clinical profiles; more bleeding episodes)
- Lower evidentiary thresholds for approval, while perhaps reasonable, raise stakes further in the post-approval period

NOACs and Reversal Agents: Post Approval Safety and Effectiveness Monitoring

- Data elements in post-approval use of reversal agents in Major/Life threatening bleeding:
 - Indication(s)-presenting signs/symptoms; formal assessment of risk; co-morbidities, clinical covariates;
 - Treatment(s)-reversal agents; other treatment for bleeding; other medical/surgical treatments
 - Outcomes-pharmacokinetic, pharmacodynamic, clinical, resource use; short- and long-term
 - System factors: time to treatment, delays, use of protocols
- Data elements in assessing broader impact of approval of reversal agents:
 - Trend in NOAC prescribing: bleeding events, changes in age, co-morbidities etc
 - Looking for evidence of off-label use of reversal agents—minor bleeding, convenience
 - Data for pharmacoeconomic analysis: service utilization, costs, PROs
- Lessons from Quality Improvement:
 - Consider standardizing protocols to develop baseline levels of performance, then refine
 - Consider a formal, dynamic learning collaborative in addition to usual study designs