

PCORI Stakeholder Workshop
New Oral Anticoagulants Questions

NOACs versus Warfarin

1. What are the differences in thrombosis and bleeding rates between new oral anticoagulants (as a group or a specific agent) versus self-monitored/telemedicine-adjusted warfarin?
 - a. In patients (women) with atrial fibrillation
 - b. In patients with VTE
 - c. In patients who have undergone surgery for knee and hip replacement
 - d. In African-American, Asian American, Hispanic, and Native American patients with atrial fibrillation
 - e. In patients with atrial fibrillation depending on their age bracket (roughly 35-54, 55-64, 65-74, 75-79, 80+)
 - f. In patients with atrial fibrillation and end stage renal disease +/- dialysis (Warfarin vs. Apixaban 5 or 2.5)
 - g. In patients with AF or history of venous thromboembolism on anticoagulation who are well controlled on a vitamin K antagonist defined as having a time in therapeutic range >65% for the past year.
 - h. In patients with AF stratified by CHA2DS2-VASc score (0 = low, 1 = intermediate, 2 or higher = high)
 - i. In patients with AF stratified by the quality of anticoagulation in patients currently on warfarin (% TTR, <55 = low, 55 -65 = intermediate, and >65 = high)
 - j. In Whites vs. non Whites (Blacks/Hispanic, and Asians)
 - k. Warfarin in AF vs the NOAC in patients with CYP2C9 polymorphism (wild type vs. CYP2C9*2/CYP2C9*3)
 - l. In patients with cancer associated thrombosis (CAT)
2. What are the differences in thrombosis and bleeding rates in low body weight (i.e., < 60 kg) and high body weight (i.e., > 120 kg) patients with venous thromboembolism? Atrial fibrillation?
3. What are patients' preferences and priorities / goals of treatment with NOACs vs warfarin for:
 - Treatment of nonvalvular atrial fibrillation (NVAf)
 - Treatment of venous thromboembolism (VTE) (defined as a DVT or PE)
 - Prevention of VTE in orthopaedic replacement surgery (ORS) (defined as total knee replacement or total hip replacement)?
4. What are the risks of bleeding between new oral anticoagulants (as a group or a specific agent) versus each other and/or versus warfarin when added to aspirin and a P2Y12 inhibitor (clopidogrel, prasugrel, or ticagrelor) in patients with acute coronary syndromes requiring stent placement and an indication for therapeutic anticoagulation?
5. What are the comparative adherence rates amongst patients with AF, DVT, VTE on warfarin versus NOACs in a real world setting and what is the impact of adherence on harms and benefits such as stroke, systemic embolisms, bleeding events?
6. What patient characteristics or factors are associated with benefits or harms for a population with AF, DVT, or VTE that switch from warfarin to a NOACs?

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7. What are the comparative benefits and harms among the NOACs:
 - a. In patients with AF and other cardiac issues such as Intra-Cardiac thrombus, Hypertrophic Cardiomyopathy and Heart Failure
 - b. In patients with VTE
 - c. In patients who have undergone surgery for knee and hip replacement
 - d. In patients with AF having procedures such as AF Ablation, Device Implantation, Hemofiltration and Dialysis
 - e. In patients with suspected or conformed Heparin-induced thrombocytopenia
 - f. In special population patients (geriatric, renal dysfunction) with atrial fibrillation?
 - g. In patients with VTE
 - h. In special population patients (geriatric, obese) who have undergone surgery for hip and knee replacement
 - i. In patients with left ventricular dysfunction as defined by ejection fraction $\leq 40\%$ and no current indication for anticoagulation
 - j. For stroke prevention in atrial fibrillation when
 - (a) Stratified and reported in aggregate across a priori subgroups; and
 - (b) When data are analyzed at a patient level to create profiles of individuals with better (or worse) response to treatment
 - k. In women on oral contraceptives or hormone replacement therapy with a DVT
 - l. For stroke prevention in non-valvular atrial fibrillation in women over the age 75 and no prior history of stroke or TIA as represented by residual stroke risk?
 - m. For incident stroke prevention in non-valvular atrial fibrillation in males and females with no prior history of history of stroke or TIA and with 100kg body weight?
8. What is the clinical impact of sex-related differences in safety using the new oral anticoagulants in patients treated for VTE using the new oral anticoagulants?

Dosing Strategies

9. What are the comparative safety and effectiveness of standardized perioperative strategies (stopping warfarin and bridging with enoxaparin OR switching to NOAC temporarily OR stopping NOAC and restarting) for anticoagulation in patients with nonvalvular atrial fibrillation who are undergoing invasive procedures?

Alternative strategies

10. What are the most effective patient engagement strategies to encourage adherence/persistence to OAC therapy? What is the impact of patient out-of-pocket costs for OACs on adherence/persistence?
11. Does dose adjustment using blood levels improve bleeding rates for patients prescribed NOAC?

NOAC vs. LMWH

12. What are the comparative benefits and harms of the NOACs compared to LMWHs for extended treatment in patients with venous thromboembolism and active cancer?