Overview: Rivaroxaban for Thromboprophylaxis in Patients Undergoing Hip or Knee Replacement Surgery

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FDA Presentations

- FDA background for the application
  - Kathy Robie Suh, M.D., Ph.D., OODP
- Rivaroxaban Efficacy and Safety
  - Min Lu, M.D., OODP
- Statistical concerns for efficacy
  - Qing Xu, Ph.D., OTS/OB
- Hepatotoxicity Concerns
  - Kate Gelperin, M.D., OSE
- Dose Adjustment Considerations
  - Christoffer Tornoe, PhD, OCP

Thromboprophylaxis in Orthopedic Surgery

- ~ 800,000 patients in US undergo Hip or knee replacement (2005 AAOS statement)
- VTE rate ~ 40-60% without prophylaxis
- Symptomatic PE or death very uncommon
- Imaging endpoints in clinical trials
- Proximal DVT generally more important than distal DVT

Drugs Approved for VTE Prophylaxis in Hip and/or Knee Surgery Patients

Drug	Indication	Treatment Duration
Enoxaparin	Hip & Knee	7 to 10 days
	Hip, extended prophylaxis	35 days
Dalteparin	Hip	5 to 10 days
Fondaparinux	Hip & Knee	5 to 9 days

Issues to Consider

- **Efficacy:**
  - Imaging (venography) endpoints accepted
- **Safety:**
  - Enoxaparin and liver test abnormalities
  - "Fixed" dose & "special populations"
- **Regulatory:**
  - Drugs currently available, all parenteral
  - First oral anticoagulant since warfarin
  - Potential "extended prophylaxis" or other use
  - On-going studies assess extended use