Clot Between a Rock and a Hard Place
The use of novel oral anticoagulants in special populations
Cam-Tu Nguyen, PharmD, BCPS
October 22nd, 2017

Disclosure Statement
I have no conflicts of interest to report related to the contents of this presentation

Objectives

Pharmacist Objectives
- Formulate an evidence based plan for management of anticoagulation in cancer associated thrombosis
- Describe pharmacokinetic changes of novel oral anticoagulants in obesity
- Compare novel oral anticoagulant options in patients with renal impairment

Technician Objectives
- List indications for novel oral anticoagulants
- Identify key differences between the novel oral anticoagulants
- Discuss patient characteristics that guide selection of oral anticoagulants

Cancer Associated Thrombosis
Obesity
Renal Impairment

Cancer Associated Thrombosis (CAT)
- Cancer associated thrombosis (CAT): venous thromboembolic (VTE) disease in patients with active cancer or cancer within previous six months
- Documented by Armand Trousseau and known as Trousseau’s Syndrome
- Malignancy leads to 4-7 fold increase in risk of VTE
- ~4-20% of cancer patients will experience CAT
- One in five VTE cases in the US is cancer associated
- Frequency of CAT is expected to rise

Cancer Associated Thrombosis
Pathogenesis

Vascular compression
Hospitalization
Decreased mobility

Stasis

Chemotherapy
Central venous catheters
Direct tumor invasion

Vessel wall injury

Hypercoagulability

Overexpression of hemostatic proteins
Inflammatory cytokines

Risk Factors for Cancer Thrombosis

Patient Related
- Gender
- Age
- Comorbidities

Treatment Related
- Chemotherapy
- Central venous catheters
- Hospitalization

Cancer Related
- Cancer stage
- Tumor site
- Time from diagnosis

Goals of CAT Treatment

- Consequences of VTE in cancer patients
  - Increased morbidity
  - Increased risk of mortality
  - Recurrent VTE
  - Increased healthcare cost
- Goals of care
  - Prevent fatal pulmonary embolism
  - Reduce morbidity
  - Minimize side effects
  - Improve quality of life

VTE Treatment Options

Treatment for VTE in the general population

- Low Molecular Weight Heparin (LMWH)
- Vitamin K Antagonist (VKA)
- Novel Oral Anticoagulants (NOACs)
- Factor Xa Inhibitors
- Direct Thrombin inhibitors

The CLOT Trial

Primary Outcome: First episode of documented, symptomatic, recurrent VTE (deep-vein thrombosis, pulmonary embolism or both)

Multicenter, randomized, open label clinical trial randomizing cancer patients with VTE or PE to LMWH or VKA
The CLOT Trial

- LMWH was more effective than VKA in reducing recurrence of VTE for six months
- 27 patients in the LMWH arm vs. 53 patients in the VKA arm
- Risk reduction of 52% in the LMWH arm compared to VKA arm
- HR 0.48 (95% CI 0.3-0.77, \(p=0.002\))


All Cause Mortality

- No statistical difference between OAC vs. LMWH
- In the dalteparin arm 130 patients (39%) vs. 136 patients (41%) in the OAC arm
- All Cause Mortality
- No statistical difference between OAC vs. LMWH
- In the dalteparin arm 19 patients (6%) vs. 12 patients (4%) in the OAC arm


LMWH vs. VKA in Cancer Thrombosis

<table>
<thead>
<tr>
<th>Clinical Trial</th>
<th>N</th>
<th>Non-VKA Treatment Arm</th>
<th>Follow Up Duration</th>
<th>Major Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>CANTHANOX</td>
<td>146</td>
<td>Enoxaparin 1.5 mg/kg daily</td>
<td>3 months</td>
<td>LMWH is as effective as VKA</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>No difference in major bleeding</td>
</tr>
<tr>
<td>LITE</td>
<td>200</td>
<td>Tinzaparin 175 u/kg daily</td>
<td>3 months</td>
<td>LMWH more effective than VKA</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>No difference in major bleeding</td>
</tr>
<tr>
<td>CATCH</td>
<td>817</td>
<td>Tinzaparin 175 u/kg daily</td>
<td>6 months</td>
<td>LMWH as effective as VKA</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>LMWH had lower rates of non-major bleeding</td>
</tr>
</tbody>
</table>

Primary outcome evaluated were VTE recurrence
All trials compared LMWH to VKA (titrated to INR goal of 2-3)

LMWH vs. VKA in Cancer Thrombosis

<table>
<thead>
<tr>
<th>Clinical Trial</th>
<th>Anticoagulant</th>
<th>CAT patients % (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>EINSTEIN-DVT</td>
<td>Rivaroxaban</td>
<td>6.8 (118)</td>
</tr>
<tr>
<td>EINSTEIN-PE</td>
<td>Rivaroxaban</td>
<td>4.7 (114)</td>
</tr>
<tr>
<td>RE-COVER I</td>
<td>Dabigatran</td>
<td>5.0 (64)</td>
</tr>
<tr>
<td>RE-COVER II</td>
<td>Dabigatran</td>
<td>3.9 (50)</td>
</tr>
<tr>
<td>AMPLIFY</td>
<td>Apixaban</td>
<td>2.5 (166)</td>
</tr>
<tr>
<td>HOKUSAI-VTE</td>
<td>Edoxaban</td>
<td>9.2 (378)</td>
</tr>
</tbody>
</table>

Definition of active cancer was not consistent across trials

Cancer Population in NOAC Trials

<table>
<thead>
<tr>
<th>Clinical Trial</th>
<th>Anticoagulant</th>
<th>CAT patients % (n)</th>
</tr>
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</tbody>
</table>

NOACS in CAT: Meta-Analysis

- Not based off of individual patient data
- Captures most landmark VTE clinical trials for NOACs

<table>
<thead>
<tr>
<th>Meta-Analysis</th>
<th>Trials</th>
<th>Patients</th>
<th>NOAC Trials Evaluated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vedovati et al. (2015)</td>
<td>6</td>
<td>1,132</td>
<td>2 Dabigatran, 2 Rivaroxaban, 1 Apixaban, 1 Edoxaban</td>
</tr>
</tbody>
</table>
Meta-Analysis: Vedovati et al. 2015

In CAT patients NOACs were associated with a non-significant reduction in VTE recurrence as compared to VKAs.

Meta-Analysis: Vedovati et al. 2015

In CAT patients NOACs were associated with a non-significant reduction in major bleeding as compared to VKAs.

Rivaroxaban Prospective Cohort Study

<table>
<thead>
<tr>
<th>Study Design</th>
<th>N</th>
<th>Intervention</th>
<th>Follow up time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prospective Cohort Study</td>
<td>200</td>
<td>Rivaroxaban 10mg PO BID x 21 days - Rivaroxaban 20mg daily for 6 months*</td>
<td>3 months</td>
</tr>
</tbody>
</table>

Primary outcome:
- Recurrent VTE
- Major Bleeding
- Non-major clinically relevant bleed
- Death from any cause

Results:
- Recurrent VTE: 4.4%
- Major Bleeding: 2.2%
- Non-major clinically relevant bleed: 3.8%
- Death from any cause: 17.6%

Major Conclusions: Rivaroxaban may be effective for treatment of CAT. Similar rate of recurrent VTE ~5% as found in EINSTEIN subgroup analysis & lower rates than observed in OAC arm of CLOT trial.

Rivaroxaban Retrospective Cohort Study

<table>
<thead>
<tr>
<th>Study Design</th>
<th>N</th>
<th>Intervention</th>
<th>Follow up time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Retrospective Cohort Study</td>
<td>224</td>
<td>Rivaroxaban 10mg PO BID x 21 days - Rivaroxaban 20mg daily</td>
<td>3 months</td>
</tr>
</tbody>
</table>

Primary outcome:
- Recurrent VTE

Results:
- Recurrent VTE: 4.0%
- Major Bleeding: 4.0%
- Fatal Bleeding: 0.9% (2 cases of fatal gastrointestinal bleed)
- Death from any cause: 13%

Major Conclusions: Rivaroxaban may be effective for treatment of CAT. Similar rate of recurrent VTE ~5% as found in EINSTEIN subgroup analysis & lower rates than observed in OAC arm of CLOT trial.

Current Guideline Recommendations

American Society of Clinical Oncology (ASCO) 2014
- LMWH preferred over VKA
- NOACs are not recommended

National Comprehensive Cancer Network (NCCN) 2016
- LMWH is preferred over VKA
- NOACs are not recommended

The International Initiative on Thrombosis and Cancer 2016
- LMWH preferred over VKA
- NOACs can be considered

American College of Chest Physicians (CHEST) 2016
- LMWH preferred over VKA and NOACs
- No recommendation on VKA vs. NOACs

Will We Ever Have an Answer?

<table>
<thead>
<tr>
<th>Study Design</th>
<th>N</th>
<th>Intervention</th>
<th>Follow up time</th>
</tr>
</thead>
<tbody>
<tr>
<td>CASTA-DIVA</td>
<td>Rivaroxaban vs. Dalteparin</td>
<td>Composite end point: Recurrent symptomatic VTE, worsening pulmonary vascular or venous obstruction</td>
<td>March 2018</td>
</tr>
<tr>
<td>SELECT-D</td>
<td>Rivaroxaban vs. Dalteparin</td>
<td>Recurrent VTE</td>
<td>December 2018</td>
</tr>
<tr>
<td>CONGO-11</td>
<td>Rivaroxaban vs. LMWH</td>
<td>Patient reported treatment satisfaction</td>
<td>March 2018</td>
</tr>
<tr>
<td>CANVAS</td>
<td>NOACs vs. LMWH</td>
<td>VTE at 6 months</td>
<td>September 2019</td>
</tr>
<tr>
<td>Molliax VTE- Cancer</td>
<td>Edoxaban vs. Dalteparin</td>
<td>VTE at 6 months</td>
<td>December 2017</td>
</tr>
<tr>
<td>ADAM-VTE</td>
<td>Apixaban vs. Dalteparin</td>
<td>Rate of major bleeding</td>
<td>November 2018</td>
</tr>
</tbody>
</table>

* Dose was reduced to 10mg BID followed up 15mg daily for plt ≤ 25,000 or ≥ 75 years of age.
Take Home Points

- LMWH remains first line therapy for CAT
- NOACs are likely an acceptable alternative to VKAs
- Patients should be involved in selection of anticoagulation therapy for CAT
- Future studies will elucidate the role of NOACs in CAT

Epidemiology

- Obesity: body mass index (BMI) ≥ 30 kg/m²
- Severe or morbid obesity: BMI ≥ 40 kg/m²
- Obesity is associated with the following:
  - Diabetes
  - VTE
  - Stroke
  - Anemia
  - Decreased functional capacity
- The CDC reports 36.3% of adults are obese
- In the state of Florida 26.2% of adults are obese

Pharmacokinetic Considerations in Obesity

- **Vd**
  - Lipophilic drugs → Vd increased in obese patients
  - Non-lipophilic drugs likely unaffected

- **Cl**
  - Dependent upon the blood flow to the organs clearing the drug
  - Altered renal and hepatic blood flow

- **T½**
  - Affected by Vd and Cl altered in obesity

Pharmacokinetic Properties of NOACs

<table>
<thead>
<tr>
<th>NOAC</th>
<th>Dabigatran</th>
<th>Rivaroxaban</th>
<th>Apixaban</th>
<th>Edoxaban</th>
</tr>
</thead>
<tbody>
<tr>
<td>T½ (hrs)</td>
<td>12-17</td>
<td>5-9</td>
<td>8-15</td>
<td>10-14</td>
</tr>
<tr>
<td>Bioavailability</td>
<td>3-7%</td>
<td>80%</td>
<td>80%</td>
<td>62%</td>
</tr>
<tr>
<td>Excretion</td>
<td>80% renal, 28% fecal</td>
<td>80% renal, 28% fecal</td>
<td>55% renal, 55% fecal</td>
<td>69% renal, 31% fecal</td>
</tr>
<tr>
<td>Metabolism</td>
<td>Hepatic glutathione conjugation</td>
<td>CYP2C9 &amp; CYP2J2</td>
<td>CYP 3A4 (2A, 2C, 2J, 2J1), CYP2J2, CYP3A4</td>
<td>CYP3A4</td>
</tr>
</tbody>
</table>

Pharmacokinetic Considerations in Obesity

- **Absorption**
  - Oral absorption unchanged
- **Distribution**
  - Ratio of adipose tissue to lean body mass
  - Lipophilicity of drug
  - Protein binding of drug
- **Metabolism**
  - Variable effects
  - Increased hepatic blood flow
- **Elimination**
  - Dependent on body weight and organ function
Clinical Trials: Obesity and Upper Body Weight

<table>
<thead>
<tr>
<th>Anticoagulant</th>
<th>Clinical Trial</th>
<th>Weight Category</th>
<th>n (%) Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dabigatran</td>
<td>RE-COVER I &amp; II</td>
<td>100 kg</td>
<td>540 (24.6%)</td>
</tr>
<tr>
<td></td>
<td>RE-LY</td>
<td>100 kg</td>
<td>3099 (17.1%)</td>
</tr>
<tr>
<td>Rivaroxaban</td>
<td>EINSTEIN-PE &amp; DVT</td>
<td>100 kg</td>
<td>590 (14.2%)</td>
</tr>
<tr>
<td></td>
<td>ROCKET-AF</td>
<td>&gt; 90 kg</td>
<td>2035 (28.5%)</td>
</tr>
<tr>
<td></td>
<td>BMI &gt; 35 kg/m²</td>
<td>972 (13.6%)</td>
<td></td>
</tr>
<tr>
<td>Apixaban</td>
<td>AMPLIFY</td>
<td>&gt; 100 kg</td>
<td>522 (19.4%)</td>
</tr>
<tr>
<td></td>
<td>BMI &gt; 35 kg/m²</td>
<td>349 (13%)</td>
<td></td>
</tr>
<tr>
<td>Edoxaban</td>
<td>ENGAGE-AF</td>
<td>None</td>
<td>611 (14.8%)</td>
</tr>
</tbody>
</table>


Dabigatran: PK/PD Data

- RE-LY sub-study prespecified
- 9,183 patients for PK/PD analysis
- Peak and trough levels one month post randomization
- Trough levels -21% lower in patients >100kg

There is an inverse relationship between dabigatran trough and patient weight.

Sub-group Analysis: Dabigatran

RE-COVER TRIAL
- Mean weight 85.5 kg (weight range: 38-175 kg)
- Subgroup analysis by weight > 100 kg failed to show significant differences in efficacy or safety outcomes

RE-LY TRIAL
- Mean weight 82.6 kg (weight range: 32-222 kg)
- Subgroup analysis by weight > 100 kg failed to show significant differences in efficacy or safety outcomes

Reported Dabigatran Treatment Failures in Obese Patients

- Patient weighing 153 kg (BMI 44.7 kg/m²): suffered ischemic stroke and undetectable dabigatran levels
- Patient weighing 124 kg (BMI 39.6 kg/m²): suffered ischemic stroke and low dabigatran levels


Rivaroxaban PK/PD Data

- Adults > 120 kg compared to normal weight group
- No difference in Cmax
- No difference in AUC
- No difference in half-life
- Few (n=81) patients had weight > 140 kg -> limited generalizability to this population

EINSTEIN DVT & PE TRIALS
- Subgroup analysis showed the primary efficacy outcomes were similar across weight groups (≤70 kg, 70-90 kg and >90 kg)
- Safety outcomes from this subgroup are not reported

Sub-group Analysis: Rivaroxaban

EINSTEIN DVT & PE TRIALS
- Obese male (BMI 39.6 kg/m²) failed dabigatran therapy for stroke prevention in AF → rivaroxaban 20 mg daily was substituted for dabigatran. Five days after initiation, rivaroxaban concentrations measured with DiXal® Direct factor Xa inhibitor were found to be within therapeutic range.

- Safety outcomes from this subgroup are not reported

Case report by Safouris A. et al.: Obese male (BMI 39.6 kg/m²) failed dabigatran therapy for stroke prevention in AF → rivaroxaban 20 mg daily was substituted for dabigatran. Five days after initiation, rivaroxaban concentrations measured with DiXal® Direct factor Xa inhibitor were found to be within therapeutic range.

Apixaban: PK/PD data

- Adults > 120 kg compared to normal weight group
- 31% lower Cmax
- 23% lower AUC
- 24% higher Xa half-life 3 hours shorter
Sub-group Analysis: Apixaban

**AMPLIFY Trial**
- Efficacy of apixaban were consistent across weight (≤ 60kg, >60-100 kg, ≥ 100 kg) and BMI (>25-30 kg/m², >30-35 kg/m², > 35 kg/m²).
- Major bleeding was significantly lower in patients with BMI > 35 kg/m², suggesting possibly due to lower drug exposure.

**ARISTOTLE Trial**
- No significant interaction between BMI and efficacy outcomes was noted.
- Reduction in bleeding rates with apixaban vs. warfarin was smaller in obese patients as compared to normal BMI.

Sub-group Analysis: Edoxaban

**Hokusai-VTE Trial**
- In subgroup analysis by body weight the primary efficacy and safety outcomes remained consistent across weight groups (≤ 60kg, >60-100 kg, > 100 kg).

**ENGAGE AF-TIMI 48**
- Trial did not report the proportion of obese patients & subgroup analysis of body weight was not performed.
- In patients with atrial fibrillation and CrCl > 95 ml/min edoxaban showed reduced efficacy → be mindful of CrCl in obese patients.

International Society on Thrombosis and Hemostasis Guidance

- Standard NOAC dosing should be used for patient with BMI < 40 kg/m² and weight ≤ 120 kg.
- NOACs should not be used in patients with BMI > 40 kg/m² or weight > 120 kg.
- If NOACs are used in patients with BMI > 40 kg/m² or weight > 120 kg we suggest checking drug specific levels.

Take Home Points

- Law numbers of severely obese (BMI > 40 kg/m²) patients are enrolled in clinical trials → AVOID ALL NOACs in this population.
- Consider use of rivaroxaban and apixaban in obese patients.
- No significant PK differences in patients with upper body weight.
- Dabigatran has shown decreased efficacy in patients with BMI > 35 kg/m² and weight > 100 kg → AVOID dabigatran in this population.

Epidemiology

- The CDC reports 30 million people (~15%) have chronic kidney disease (CKD).
- Estimated 660,000 Americans are being treated for end stage renal disease (ESRD).
- 468,000 dialysis dependent.
- Patients with CKD or ESRD:
  - Increased risk of thromboembolic events
  - Increased risk of bleeding
- NOAC trials underrepresent this patient population.

Cancer Associated Thrombosis

Obesity

Renal Impairment
Renal Impairment in Clinical Trials

- **Rivaroxaban**: Excluded CrCl < 30 ml/min
- **Edoxaban**: Excluded CrCl < 30 ml/min
- **Apixaban**: Excluded CrCl < 25 ml/min
- **Dabigatran**: Excluded CrCl < 30 ml/min

**Recommended Renal Dose Adjustments**

<table>
<thead>
<tr>
<th>Anticoagulant</th>
<th>AF Dose</th>
<th>AF Renal Adjustment</th>
<th>VTE Dose</th>
<th>VTE Renal Adjustment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dabigatran</td>
<td>150 mg BID</td>
<td>CrCl &lt; 30 ml/min: 75mg BID, CrCl &lt; 15 ml/min: do not use</td>
<td>Parenteral x 5 days then 150 mg BID</td>
<td>CrCl &lt; 10 ml/min do not use</td>
</tr>
<tr>
<td>Rivaroxaban</td>
<td>20 mg daily</td>
<td>CrCl &lt; 50 ml/min: 15mg daily, CrCl &lt; 15 ml/min: do not use</td>
<td>Parenteral x 3 weeks then 20 mg daily</td>
<td>CrCl &lt; 10 ml/min do not use</td>
</tr>
<tr>
<td>Apixaban</td>
<td>5 mg BID</td>
<td>2.5 mg BID if two of three are met: Age &gt; 80 years, &lt; 60 kg, Scr &gt; 1.5 mg/dL</td>
<td>10mg BID x 1 week then 5mg BID</td>
<td>CrCl &lt; 10 ml/min do not use</td>
</tr>
<tr>
<td>Edoxaban</td>
<td>60 mg daily</td>
<td>CrCl &lt; 50 ml/min: 30mg daily, CrCl &lt; 15 ml/min: do not use</td>
<td>Parenteral x 5 days then 60 mg daily</td>
<td>CrCl &lt; 15 ml/min do not use</td>
</tr>
</tbody>
</table>

**Review of Evidence: NOACs in ESRD**


**Apixaban in Hemodialysis Patients**
Apixaban in ESRD

- The only NOAC FDA approved for patients on hemodialysis (HD)
- AF indication only
- Same dose reduction criteria as non-ESRD patients

Single Dose Pharmacokinetic Study

ESRD Patients
- 36% higher AUC
- No difference in half-life

Apixaban in ESRD

Pharmacokinetic Study of Apixaban at Steady State in HD Patients

- 2.5 mg group: Significant increased in AUC and drug trough levels
- 5 mg group: Trough levels increased to greater than the 90th percentile observed in healthy adult patients
- 5 mg twice daily should be avoided in HD patients

Apixaban in ESRD

Comparison of the Safety and Effectiveness of Apixaban versus Warfarin in Patients with Severe Renal Impairment

<table>
<thead>
<tr>
<th>Study Design</th>
<th>Patient Population</th>
<th>N</th>
<th>Study Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Retrospective matched-cohort</td>
<td>Peritoneal dialysis or hemodialysis or Scr = 2.5 mg/dL or CrCl = 25 ml/min</td>
<td>146</td>
<td>2 years</td>
</tr>
</tbody>
</table>

- Renal Impairment: 27.4% ESRD on HD, 9.6% ESRD not on HD, 43.9% CrCl < 25 ml/min or Scr = 2.5 mg/dL
- Indication for anticoagulation: 72.6% - AFIB, 26% - VTE, 1.4% - Other
- No statistically significant differences regarding major bleeding in dialysis patients (p=0.74)
- No efficacy outcomes reported specifically for HD group

Apixaban in ESRD: What is in the Pipeline?

1. RENAL-AF
   - Treatment Arms: Apixaban vs. VKA
   - Primary Outcome: Time to first major bleeding or non-major bleeding event
   - Estimated Completion: May 2019

2. AXADIA
   - Treatment Arms: Apixaban vs. VKA
   - Primary Outcome: Major, clinically relevant, and non-major bleeding
   - Estimated Completion: April 2019

Rivaroxaban in ESRD

- Currently not FDA approved for use in ESRD patients
- Avoid in AF population if CrCl < 15 ml/min
- Avoid in VTE population if CrCl < 30 ml/min
- Dual elimination via hepatic P450 system and renal elimination
- Highly protein bound → Limits ability to be dialyzed
Rivaroxaban in ESRD

**Single Dose Pharmacokinetic Study**

- Post-HD dose of rivaroxaban resulted in 56% higher AUC than observed in healthy adults.
- Rivaroxaban was minimally removed by hemodialysis.

**Take Home Points**

- Rivaroxaban, dabigatran, and edoxaban should be avoided in ESRD patients.
- Apixaban is the only FDA approved NOAC for use in HD patients with AF.
- Scrutinize apixaban dosing for patients on HD.
- Be mindful of dose adjustments for all NOACs in patients with CKD.

**Assessment Question 1**

What is the anticoagulant of choice for patients with cancer associated thrombosis?

- A. LMWH
- B. Warfarin
- C. Apixaban
- D. Edoxaban

**Assessment Question 2**

VG is a 66 year old female (height 5’9”, weight 210 lbs, BMI 31 kg/m²) with no PMH who is diagnosed with new on set atrial fibrillation. VG will be discharged today and the medical team asked pharmacy to pick the anticoagulant – which of the following NOACs is appropriate?

- A. Dabigatran
- B. Apixaban
- C. Rivaroxaban
- D. B&C

**Assessment Question 3**

BR is a 59 year old male on hemodialysis. BR has been on warfarin for stroke prevention in the setting of AFIB for 3 years but is no longer able to make appointments for INR monitoring. The patients requests an oral anticoagulant that requires less monitoring.

Which of the following NOACs could be used for this patient?

- A. Rivaroxaban
- B. Dabigatran
- C. Apixaban
- D. Edoxaban

**Clot Between a Rock and a Hard Place**

The use of novel oral anticoagulants in special populations

Cam-Tu Nguyen PharmD, BCPS
October 22nd, 2017
In CAT patients NOACs were associated with a non-significant reduction in VTE recurrence as compared to VKAs.
Bariatric Surgery Patients

**Table: Characteristics of Oral Anticoagulants**

| Anticoagulant | Mark | Location of Absorption | Volume of Distribution | \( \text{t} \ | \) |
|---------------|------|------------------------|------------------------|-------|
| Nadroparin    | Exogenous | Upper small intestine, some gastric absorption | 101 L (3-3.5 L) | 11.5 h |
| Indaparine    | Endogenous | Lower small intestine | 50-10 L (0.5-1 L) | 13 h |
| Enoxaparin    | Endogenous | Proximal small intestine | 38 L (0.5-1 L) | 11.5 h |
| Rivaroxaban   | Endogenous | Proximal small intestine, some gastric absorption | 18-1 (0.1-0.2 L) | 11.5 h |
| Warfarin      | Endogenous | Proximal gastric system | 6.34 L (0.8-3 L) | 1 |

**Rivaroxaban in ESRD**

Dose Finding Study of Rivaroxaban in Hemodialysis Patients

- AUC increased on average 1.7 fold as compared to healthy volunteers
- Cmax and T1/2 were unchanged as compared to healthy volunteers

N=12

N=12

N=6