They’re Not So New Anymore...Update on NOAC’s (Novel Oral Anticoagulants)

Daniel B. DiCola, MD

Paul W. Ament, PharmD
Daniel DiCola, MD
ddicola@excelahealth.org

• Faculty:
  – Latrobe Area Hospital, Excela Health Family Medicine Residency
  – Clinical Associate Professor, Family and Community Medicine, Sidney Kimmel Medical College at Thomas Jefferson University
Conflicts of Interest

• None
Goals

• Compare VKA (Vitamin K+ antagonist-Warfarin) and LMW (Heparin) with the novel oral anticoagulants (NOACs) (Apixaban, Dabigatran, Edoxaban, Rivaroxaban) in chronic atrial fibrillation and elective orthopedic prophylaxis and treatment of thromboembolic disease

• Review topics from the CHEST Guidelines that family doctors use daily in their practices.
• Review Evolution of New Indications for NOACs

• Review Status of Reversal Agents for NOACs

• NOAC versus NOAC
• Review Common Anticoagulation Conditions where NOACs may not be the Best Agent

• Case Presentations
What is an Ideal Anticoagulant?
Table 2
Comparison of “ideal anticoagulant”, warfarin, and other new promising oral anticoagulants.

<table>
<thead>
<tr>
<th></th>
<th>Ideal anticoagulant</th>
<th>Warfarin</th>
<th>Ximelagatan</th>
<th>Dabigatran</th>
<th>Rivaroxaban</th>
<th>Apixaban</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Target on coagulation system</strong></td>
<td>Selective</td>
<td>Non-selective (Vitamin K-dependent factors: II, VII, IX, X)</td>
<td>Thrombin (factor IIa)</td>
<td>Thrombin (factor IIa)</td>
<td>Factor Xa</td>
<td>Factor Xa</td>
</tr>
<tr>
<td><strong>Dosing</strong></td>
<td>Fixed, once daily</td>
<td>Variable, once daily</td>
<td>Fixed, once daily</td>
<td>Fixed, twice daily</td>
<td>Fixed, once daily</td>
<td>Fixed, twice daily</td>
</tr>
<tr>
<td><strong>Bioavailability, %</strong></td>
<td>High</td>
<td>20</td>
<td>6.5</td>
<td>60–80</td>
<td>&gt;50</td>
<td></td>
</tr>
<tr>
<td><strong>Onset of action, hours</strong></td>
<td>Short</td>
<td>2</td>
<td>2</td>
<td>3</td>
<td>3</td>
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<tr>
<td><strong>Half-life, hours</strong></td>
<td>Short</td>
<td>40</td>
<td>14–17</td>
<td>9</td>
<td>9–14</td>
<td></td>
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<tr>
<td><strong>Renal clearance, %</strong></td>
<td>Minimal</td>
<td>80</td>
<td>80</td>
<td>65</td>
<td>25</td>
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<tr>
<td><strong>Common side effects</strong></td>
<td>No</td>
<td>High risk of major bleeding (2.3%/year)</td>
<td>Elevated liver enzyme levels (about 6%)</td>
<td>Dyspepsia (5–6%)</td>
<td>Unknown</td>
<td>Unknown</td>
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<tr>
<td><strong>Food and drug interactions</strong></td>
<td>No</td>
<td>Vitamin K-containing food, multiple medications</td>
<td>Minimal</td>
<td>Minimal</td>
<td>Potent CYP3A4 inhibitors</td>
<td>Potent CYP3A4 inhibitors</td>
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<tr>
<td><strong>Safety to use in pregnancy</strong></td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td><strong>Need for coagulation test</strong></td>
<td>No</td>
<td>Yes (INR 2–3)</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
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<tr>
<td><strong>Antidote(s)</strong></td>
<td>Yes</td>
<td>Yes (Vitamin K or fresh frozen plasma)</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
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<tr>
<td><strong>Long-term safety data</strong></td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
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<tr>
<td><strong>Cost-effectiveness</strong></td>
<td>Yes</td>
<td>Unknown</td>
<td>Unknown</td>
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</table>

INR = international normalized ratio.

a Still pending results from randomized control studies in patients with atrial fibrillation.
b Including macrolide, ketoconazole and protease inhibitors.
An Ideal Anticoagulant

- Infrequent or No Monitoring
- One Size Fits All – Fixed Dose
- Minimal Drug Interactions
- Minimal Food Interactions
- Oral – Quick Onset
An Ideal Anticoagulant

- 100% Effective
- Reversible – Specific Antidote
- Once Daily
- Low Incidence of Heparin Induced Thrombocytopenia (HIT)
An Ideal Anticoagulant

- Specific Antidote – Rapid
- No Evidence of Hypercoagulability
- No Need for Bridging
- Selective
Periprocedural Anticoagulation Management of Patients with Thrombophilia

Ewa M. Wysokinska, MD, Waldemar E. Wysokinski, MD, PhD, Siva Ketha, MD, Scott Litin, MD, Paul Daniels, MD, Joshua Slusser, BS, David O. Hodge, MS, John A. Heit, MD, Robert D. McBane II, MD
An Ideal Anticoagulant

• Clearance – Multi-Organ Clearance
• Long-term Safety Data
Coumadin, the Devil We Know

it’s time to introduce our newest sun devil

welcome TOTT GRAHAM
• Warfarin is Under Prescribed

• Admissions for Drug Toxicity – Coumadin Always in Top 5
Evaluation of Dose-Reduced Direct Oral Anticoagulant Therapy

Megan E. Barra, PharmD, John Fanikos, RPh, MBA, Jean M. Connors, MD, Katelyn W. Sylvester, PharmD, Gregory Piazza, MD, MS, Samuel Z. Goldhaber, MD
Atrial Fibrillation
Validation of risk stratification schemes for predicting stroke and thromboembolism in patients with atrial fibrillation: nationwide cohort study

Jonas Bjerring Olesen, research fellow; Gregory Y H Lip, professor; Morten Lock Hansen, research fellow; Peter Riis Hansen, research director; Janne Schurmann Tolstrup, research director; Jesper Lindhardsen, research fellow; Christian Selmer, research fellow; Ole Ahlehoff, research fellow; Anne-Marie Schjerning Olsen, research fellow; Gunnar Hilmar Gislason, research director; Christian Torp-Pedersen, professor
<table>
<thead>
<tr>
<th>C</th>
<th>H</th>
<th>A₂</th>
<th>D</th>
<th>S₂</th>
<th>V</th>
<th>A</th>
<th>S_c</th>
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<tbody>
<tr>
<td>C</td>
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<td>N</td>
<td>E</td>
<td>E</td>
<td>K</td>
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<td>C</td>
<td>M</td>
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<td>&gt;</td>
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<td>5</td>
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</table>

Stroke Risk Based on Score
3 Major Risk Factors

• Prior Thromboembolism
• Age > 75
• DM + CHF Together
CHADS₂ versus CHA₂DS₂-VASc score in assessing the stroke and thromboembolism risk stratification in patients with atrial fibrillation: a systematic review and meta-analysis

Jia-Yuan Chen, Ai-Dong Zhang, Hong-Yan Lu, Jun Guo, Fei-Fei Wang, and Zi-Cheng Li
<table>
<thead>
<tr>
<th>Bleeding Risk Assessment Scoring Tools</th>
<th>Factors in Scoring System</th>
<th>Scoring</th>
</tr>
</thead>
</table>
| Anticoagulation and Risk Factors in Atrial Fibrillation (ATRIA) | 1 point for presence of each:  
- Bleeding history  
- Hypertension  
2 points for presence of:  
- Age ≥ 75  
3 points for presence of each:  
- Anemia  
- Severe renal failure | Low: 0–3  
Moderate: 4  
High: 5–10  
*Maximum of 10 points* |
| HAS-BLED | 1 point for presence of each:  
- Hypertension  
- Abnormal renal/liver function (2 pts for both)  
- Stroke  
- Bleeding history  
- Predisposition  
- Labile INRs  
- Drug therapy/alcohol intake (2 pts for both) | Low: 0  
Moderate: 1–2  
High: ≥ 3  
*Maximum of 9 points* |
| HEMORR,HAGES | 1 point for each risk factor present:  
- Hepatic or renal disease  
- ETOH abuse (ethyl alcohol)  
- Malignancy  
- Age >75 years  
- Reduced platelet count or function  
- Rebleeding risk*  
- Hypertension (uncontrolled)  
- Anemia  
- Genetic factors (CYP2C9)  
- Excessive fall risk  
- Stroke  
*2 points for previous bleed | Low: 0  
Moderate: 2–3  
High: ≥ 4  
*Maximum of 12 points* |
| Outpatient Bleeding Risk Index (OBRI) | 1 point for presence of each condition and 0 if absent:  
- Age ≥ 65 years  
- GI bleed in past 2 weeks  
- Previous stroke  
- Comorbidities (recent MI, Hct < 30%, diabetes, creatinine > 1.5 mg/dL) | Low: 0  
Moderate: 1–2  
High: ≥ 3  
*Maximum of 4 points* |

Hct = hematocrit; MI = myocardial infarction.
The HAS-BLED Score Has Better Prediction Accuracy for Major Bleeding Than CHADS\(_2\) or CHA\(_2\)DS\(_2\)-VASc Scores in Anticoagulated Patients With Atrial Fibrillation

Vanessa Roldan, MD, PhD; Francisco Marín, MD, PhD; Sergio Manzano-Fernandez, MD, PhD; Pilar Gallego, MD; Juan Antonio Vilchez, PhD; Mariano Valdes, MD, PhD; Vicente Vicente, MD, PhD; Gregory Y.H. Lip, MD

[+ ] Author Information

<table>
<thead>
<tr>
<th>HAS-BLED</th>
<th>1 point for presence of each:</th>
<th>Low: 0</th>
<th>Moderate: 1–2</th>
<th>High: ≥ 3</th>
<th>Maximum of 9 points</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Hypertension</td>
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<tr>
<td></td>
<td>• Abnormal renal/liver function (2 pts for both)</td>
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<tr>
<td></td>
<td>• Stroke</td>
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</tr>
<tr>
<td></td>
<td>• Bleeding history</td>
<td></td>
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<tr>
<td></td>
<td>• Predisposition</td>
<td></td>
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</tr>
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<td></td>
<td>• Labile INRs</td>
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<tr>
<td></td>
<td>• Drug therapy/alcohol intake (2 pts for both)</td>
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</tbody>
</table>
The Future

- 9 Drugs in Pipeline
- Possible Uses
  - ACS
  - DVT treatment
  - PE Treatment
  - Medical Prophylaxis
Evolving use of new oral anticoagulants for treatment of venous thromboembolism

Calvin H. Yeh, Peter L. Gross and Jeffrey I. Weitz

Paul W. Ament, PharmD

pament@excelahealth.org

• **Manager**: Clinical Pharmacy, Excela Health
• **Faculty**: Latrobe Area Hospital, Excela Health Family Medicine Residency;

Associate Clinical Preceptor of Pharmaceutical Sciences in the School of Pharmacy, Department of Pharmacy and Therapeutics, University of Pittsburgh;

Adjunct Clinical Instructor in the Department of Clinical Pharmacy, Mylan School of Pharmacy, Duquesne University
Disclosure

Speakers Panel:
- Janssen
- Merck
- Pfizer
Coagulation Cascade

VKAs inhibit synthesis of FII, VII, IX, X

Factor Xa inhibitors

Direct thrombin inhibitors

Fibrinogen -> Fibrin

<table>
<thead>
<tr>
<th>ORTHOPEDIC PROPHYLAXIS</th>
<th>NON-VALVULAR A.FIB</th>
<th>ACUTE DVT / PE</th>
<th>RISK REDUCTION VTE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>APIXABAN</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.5mg BID</td>
<td>5mg BID</td>
<td>10mg BID x7 Days =&gt; 5mg BID</td>
<td>2.5mg BID</td>
</tr>
<tr>
<td>Knee x12 Days</td>
<td>2.5mg BID (2 of 3): Age &gt;80 Creat &gt;1.5mg/dl Wt &lt;60Kg ESRD (same) ** No Clinical Data CrCl &lt;30ml/min</td>
<td>** No Clinical Data CrCl &lt;30ml/min</td>
<td></td>
</tr>
<tr>
<td>Hip x35 Days</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>DABIGATRAN</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hip only</td>
<td>CrCl &gt;30ml/min 150mg BID CrCl 15-30ml/min 75mg BID</td>
<td>AFTER 5-10 Days parenteral anticoagulation 150mg BID</td>
<td>150mg BID</td>
</tr>
<tr>
<td>110mg Day 1 =&gt; 220mg QDay x28-35 Days</td>
<td>** CrCl &gt;30ml/min</td>
<td>** CrCl &gt;30ml/min</td>
<td>** CrCl &gt;30ml/min</td>
</tr>
<tr>
<td><strong>EDOXABAN</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>CrCl 50-95ml/min 60mg QDay CrCl 15-50ml/min 30mg QDay</td>
<td>AFTER 5-10 Days parenteral anticoagulation CrCl &gt;50ml/min =&gt; 60mg QDay CrCl 15-50ml/min; Wt &lt;60Kg; P-gp inhibitors =&gt; 30mg QDay</td>
<td></td>
</tr>
<tr>
<td></td>
<td>** Contraindicated with CrCl &gt;95ml/min</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>RIVAROXABAN</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10mg QDay</td>
<td>CrCl &gt;50ml/min 20mg QDay with evening meal CrCl 15-50ml/min 15mg QDay with evening meal ESRD 15mg QDay with evening meal</td>
<td>15mg BID x21 Days =&gt; 20mg QDay Take all doses with food ** No Clinical Data CrCl &lt;30ml/min</td>
<td>20mg QDay with food</td>
</tr>
<tr>
<td>Knee x12 Days</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hip x35 Days</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>** CrCl &gt;30ml/min</td>
<td></td>
<td></td>
<td></td>
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</tbody>
</table>
# Pharmacokinetic Comparison

<table>
<thead>
<tr>
<th></th>
<th>Dabigatran</th>
<th>Apixaban</th>
<th>Edoxaban</th>
<th>Rivaroxaban</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MOA</strong></td>
<td>Direct Thrombin Inhibitor</td>
<td>Factor Xa Inhibitor</td>
<td>Factor Xa Inhibitor</td>
<td>Factor Xa Inhibitor</td>
</tr>
<tr>
<td><strong>Bioavailability</strong></td>
<td>6-8%</td>
<td>50%</td>
<td>60%</td>
<td>80%</td>
</tr>
<tr>
<td><strong>Time to Peak</strong></td>
<td>2 hrs</td>
<td>3 hrs</td>
<td>1-2 hrs</td>
<td>2-3 hrs</td>
</tr>
<tr>
<td><strong>Half-life</strong></td>
<td>14-17 hrs</td>
<td>7-11 hrs</td>
<td>9-11 hrs</td>
<td>5-9 hrs (11-13 hrs elderly)</td>
</tr>
<tr>
<td><strong>Renal Excretion</strong></td>
<td>80%</td>
<td>27%</td>
<td>35-50%</td>
<td>33%</td>
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</table>
## Interactions

<table>
<thead>
<tr>
<th></th>
<th>Apix</th>
<th>Dabi</th>
<th>Edox</th>
<th>Rivarox</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Induce</strong> CYP / P-gp</td>
<td>Avoid</td>
<td>Avoid (Rifampin)</td>
<td>Avoid (Rifampin)</td>
<td>Avoid</td>
</tr>
<tr>
<td><strong>Rifampin / Carbamaz / Phenytoin / St John’s Wort</strong></td>
<td>Avoid</td>
<td>Avoid (Rifampin)</td>
<td>Avoid (Rifampin)</td>
<td>Avoid</td>
</tr>
<tr>
<td><strong>Inhibit</strong> CYP / P-gp</td>
<td>↓ Dose by 50% (avoid if on 2.5mg)</td>
<td>CrCl 30-50 ↓ 75 mg BID (Dronedarone/ Keto) (avoid if CrCl &lt;30)</td>
<td>VTE only 30mg Qday (verapamil, quinidine, macrolide, itra / keto)</td>
<td>Avoid (Conivaptan)</td>
</tr>
<tr>
<td><strong>Azoles (Keto/Itra); clarithromycin; “Vir” HIV Agents</strong></td>
<td>↓ Dose by 50% (avoid if on 2.5mg)</td>
<td>CrCl 30-50 ↓ 75 mg BID (Dronedarone/ Keto) (avoid if CrCl &lt;30)</td>
<td>VTE only 30mg Qday (verapamil, quinidine, macrolide, itra / keto)</td>
<td>Avoid (Conivaptan)</td>
</tr>
<tr>
<td><strong>Anticoag / NSAID/ Antiplatelet / SSRI / SNRI</strong></td>
<td>↑ Bleeding</td>
<td>↑ Bleeding</td>
<td>↑ Bleeding</td>
<td>↑ Bleeding</td>
</tr>
<tr>
<td><strong>Weak Inhibitor CYP / P-gp</strong></td>
<td>Risk vs Benefit CrCl &lt;80 and Azithro/ Dronedarone/ Diltiazem/Verapamil</td>
<td></td>
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</tbody>
</table>
Results: For patients with nonrheumatic AF, including those with paroxysmal AF, who are (1) at low risk of stroke (eg, CHADS$_2$ [congestive heart failure, hypertension, age $\geq$ 75 years, diabetes mellitus, prior stroke or transient ischemic attack] score of 0), we suggest no therapy rather than antithrombotic therapy, and for patients choosing antithrombotic therapy, we suggest aspirin rather than oral anticoagulation or combination therapy with aspirin and clopidogrel; (2) at intermediate risk of stroke (eg, CHADS$_2$ score of 1), we recommend oral anticoagulation rather than no therapy, and we suggest oral anticoagulation rather than aspirin or combination therapy with aspirin and clopidogrel; and (3) at high risk of stroke (eg, CHADS$_2$ score of $\geq$ 2), we recommend oral anticoagulation rather than no therapy, aspirin, or combination therapy with aspirin and clopidogrel. Where we recommend or suggest in favor of oral anticoagulation, we suggest dabigatran 150 mg bid rather than adjusted-dose vitamin K antagonist therapy.
5. For patients with nonvalvular AF with prior stroke, transient ischemic attack (TIA), or a CHA₂DS₂-VASc score of 2 or greater, oral anticoagulants are recommended. Options include warfarin (INR 2.0 to 3.0) (68-70) (Level of Evidence: A), dabigatran (74) (Level of Evidence: B), rivaroxaban (75) (Level of Evidence: B), or apixaban (76). (Level of Evidence: B)
RESULTS: For VTE and no cancer, as long-term anticoagulant therapy, we suggest dabigatran (Grade 2B), rivaroxaban (Grade 2B), apixaban (Grade 2B), or edoxaban (Grade 2B) over vitamin K antagonist (VKA) therapy, and suggest VKA therapy over low-molecular-weight heparin (LMWH; Grade 2C). For VTE and cancer, we suggest LMWH over VKA (Grade 2B), dabigatran (Grade 2C), rivaroxaban (Grade 2C), apixaban (Grade 2C), or edoxaban (Grade 2C).
## Transition to NOAC

<table>
<thead>
<tr>
<th></th>
<th>Warfarin</th>
<th>LMWH / UFH</th>
</tr>
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<tbody>
<tr>
<td><strong>Apixaban</strong></td>
<td>Initiate INR &lt; 2</td>
<td>Initiate when next scheduled dose due</td>
</tr>
<tr>
<td><strong>Dabigatran</strong></td>
<td>Initiate INR &lt; 2</td>
<td>Initiate when next scheduled dose due</td>
</tr>
<tr>
<td><strong>Edoxaban</strong></td>
<td>Initiate INR &lt;2.5</td>
<td>DC UFH x4H; Initiate when next LMWH dose due</td>
</tr>
<tr>
<td><strong>Rivaroxaban</strong></td>
<td>Initiate INR &lt;3</td>
<td>Initiate when next scheduled dose due</td>
</tr>
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## Preop Interruption (Last Dose)

<table>
<thead>
<tr>
<th>Agent</th>
<th>CrCl</th>
<th>Low Risk</th>
<th>High Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dabigatran</td>
<td>&gt;50</td>
<td>2 days</td>
<td>3 days</td>
</tr>
<tr>
<td></td>
<td>31-50</td>
<td>3 days</td>
<td>4 days</td>
</tr>
<tr>
<td></td>
<td>≤30</td>
<td>4 days</td>
<td>6 days</td>
</tr>
<tr>
<td>Apixaban</td>
<td>&gt;31</td>
<td>2 days</td>
<td>3 days</td>
</tr>
<tr>
<td></td>
<td>≤30</td>
<td>2 days</td>
<td>4 days</td>
</tr>
<tr>
<td>Edoxaban</td>
<td>&gt;31</td>
<td>2 days</td>
<td>3 days</td>
</tr>
<tr>
<td></td>
<td>≤30</td>
<td>3 days</td>
<td>4 days</td>
</tr>
<tr>
<td>Rivaroxaban</td>
<td>&gt;31</td>
<td>2 days</td>
<td>3 days</td>
</tr>
<tr>
<td></td>
<td>≤30</td>
<td>3 days</td>
<td>4 days</td>
</tr>
</tbody>
</table>

Low = Colonoscopy, Breast biopsy, minor orthopedic, cardiac cath
High = Surgery: Abdominal, Cardiac, Kidney, Neuro, Prostate, Spinal, Vascular

Bleeding Management

• Discontinue: Short $T \frac{1}{2} \Rightarrow$ Eliminated 24-48 hours

• Supportive Management
  • FFP (Does Not Reverse DTI / Xa)
  • Compress Bleeding Sites
  • Gastric Lavage / Charcoal < 3 Hours of Dose
  • ? Dialysis $\Rightarrow$ Dabigatran
**Bleeding Management**

- **Idarucizumab (Praxbind)**
  - Monoclonal Antibody
    - Binds to Dabigatran Neutralizing Effects
    - Higher Affinity to Dabi vs Thrombin
    - Near 100% Reversal at 4 hours
- **Indications:**
  - Life-threatening Bleed
  - Reversal for Urgent / Emergency Surgery
- **Dose:** 5gm IV Bolus or Infusion
- **Cost = $3,500**
Bleeding Management

- **Prothrombin Complex Concentrate (Kcentra®)**
  - FDA Approved for Warfarin Reversal
  - 25 – 50 units / kg
  - 5,000 units = $7,500

- **Andexanet**
  - Binds to Xa Molecule
  - Neutralization within Minutes
  - Phase II Studies with Xa Inhibitors / Enoxaparin
  - FDA Denied Approval August 2016
Clinical Issues

- Reversibility
- Quantitative Assay
  - Interacting Drugs
  - Extremes of Weight
  - Emergency Procedures / Surgery
- Treatment Failures
When To Use Warfarin

• Compromised Renal Function
  • Studies Excluded CrCl <25 ml/min
  • Apixaban / Rivaroxaban PI => ESRD
    • Limited Clinical Data
• Valvular Heart Disease
• DAPT
• Satisfied with Warfarin
  • If It’s Fixed Don’t Break It
# Monthly Cost

<table>
<thead>
<tr>
<th>Drug</th>
<th>Monthly Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warfarin</td>
<td>$4</td>
</tr>
<tr>
<td>Copay for INR</td>
<td>$??</td>
</tr>
<tr>
<td>Apixaban 5mg</td>
<td>$370</td>
</tr>
<tr>
<td>Dabigatran 150mg</td>
<td>$350</td>
</tr>
<tr>
<td>Edoxaban 60mg</td>
<td>$300</td>
</tr>
<tr>
<td>Rivaroxaban 20mg</td>
<td>$370</td>
</tr>
</tbody>
</table>

Retail Pricing Cardinal March 2017
BadDrug.com
Powered by 1-800-LAW-FIRM

If you suffered injuries from a dangerous drug or defective medical product, you have options.
Summary

- Simplicity
- Rapid Onset
- Paradigm Shift $\Rightarrow$ LMWH Reluctance in ’90s
- Developed as Warfarin Alternative
  - Non-Inferior $\Rightarrow$ Superior Efficacy / Safety
- NOAC’ s vs Warfarin
  - $\downarrow$ Major Bleeding
  - $\downarrow$ Intra Cranial Bleeding
  - $\downarrow$ Overall Mortality 10%
- Clinical Role is Rapidly Evolving
Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines

EXECUTIVE COMMITTEE:
Gordon H. Guyatt, MD, FCCP, Chair
Elie A. Akl, MD, MPH, PhD
Mark Crowther, MD
David D. Gutterman, MD, FCCP
Holger J. Schünemann, MD, PhD, FCCP

www.chestpubs.org
• NOAC vs NOAC—Limited Head to Head Data
• Kidney Dysfunction
• Coronary Artery Disease
• GERD
• GI Bleeding
• Antidote

• Drug Interactions

• RV Dysfunction
Efficacy and Safety of Rivaroxaban in Patients with Venous Thromboembolism and Active Malignancy: A Single-Center Registry.

Bott-Kitslaar DM¹, Saadiq RA¹, McBane RD¹, Loprinzi CL², Ashrani AA³, Ransone TR¹, Wolfgram AA¹, Berentsen MM¹, Wysokinski WE⁴.
Where Not to Use NOACs

Cancer Related DVT / PE

Renal Dysfunction

Liver Dysfunction
• Valvular Atrial Fibrillation
• Unstable Medical Patients
• Hypercoagulable State
• Extensive Clot Burden
Dabigatran versus Warfarin in Patients with Mechanical Heart Valves

John W. Eikelboom, M.D., Stuart J. Connolly, M.D., Martina Brueckmann, M.D., Christopher B. Granger, M.D., Arie P. Kappetein, M.D., Ph.D., Michael J. Mack, M.D., Jon Blatchford, C.Stat., Kevin Devenny, B.Sc., Jeffrey Friedman, M.D., Kelly Guiver, M.Sc., Ruth Harper, Ph.D., Yasser Khder, M.D., Maximilian T. Lombeyer, Ph.D., Hugo Maas, Ph.D., Jens-Uwe Voigt, M.D., Maarten L. Simoons, M.D., and Frans Van de Werf, M.D., Ph.D., for the RE-ALIGN Investigators

• $$

• Triple Therapy

• Acute Coronary Syndrome

• Pregnancy
Antithrombotic Therapy After an ACS

AF patient in need of OAC after an ACS

Bleeding risk high

Bleeding risk low

Time From ACS, mo

0 1 3 6 12+

Triple therapy*

Dual therapy (IIaC)*

OAC monotherapy

OAC monotherapy

Dual therapy (IIaC)†

*OAC + aspirin 75-100 mg/d + clopidogrel 75 mg/d;
†OAC + aspirin 75-100 mg/d OR clopidogrel 75 mg/d
BB is a generally healthy 75 yo wf who suffered an unprovoked saddle PE with RV dysfunction > than 5 years ago. She has mild hbp controlled with single agent therapy. She also has GERD, EGD proven esophagitis, which is only controlled with Nexium brand necessary requiring frequent calls for pre authorization. Her husband has rheumatoid arthritis and prostate cancer. He is maintained on immunosuppressant therapy.
Case Study

• and hormonal therapy. They fall into the donut hole each fall. She has never had an INR out of therapeutic range and comes to our Coumadin clinic. She lives 2 blocks from the hospital. She asks about switching to a NOAC??

• How often do you need to check her INR??
• *Does he need anticoagulation?? Agent ??*
Case Study

• 80 yo white male with A-fib. He suffered a MCA CVA, probable embolic due to A-fib. He lives alone, with his nearest relative residing in California. She is an RN. He can no longer drive due to visual field cuts. He had a bleeding ulcer 7 years ago with no further episodes due to lifestyle changes. Patient has HTN controlled with 1 agent
Case Study

- CK 60yr male; HX HTN, CVA, pre-diabetes, paroxysmal A. flutter, Transient SVT, ESRD on hemodialysis
- CHADS$_2$VASC = 3
- Patient adamantly refuses warfarin TX: Father was on warfarin and experienced fatal bleed
  - “I won’t take warfarin Doc…find something else”
- TX Guidelines recommend warfarin for CrCl <30ml/min
- Clinical Trials for NOACs Excluded CrCl <25ml/min
- Apixaban and Rivaroxaban PI includes ESRD
  - Apixaban 2.5mg or 5mg BID
  - Rivaroxaban 15mg QDay with food
Case Study

- 97yr male unprovoked DVT. Daughter’s want to “discuss anticoagulation options”. Patient has difficulty ambulating secondary to osteoarthritis. Patient resides with daughters x6 months (Greensburg and Scranton). Mother was on warfarin and encountered physician reluctance to manage warfarin when in different area of PA
  - “Coumadin will make dad’s life difficult, is there an easier option?”
- TX with Rivaroxaban
- Key teaching point: Listen to your patient’s needs