Acute Care:
Understanding Direct Oral Anticoagulants (DOACs)

National Conference for Nurse Practitioners (NCNP)
October 11, 2017

John Togami, PharmD, PhC
Pharmacist Clinician - Outpatient Anticoagulation Services
University of New Mexico Hospitals
Clinical Assistant Professor – University of New Mexico College of Pharmacy
jtogami@salud.unm.edu

Objectives

- Discuss the efficacy and safety of DOACs compared to conventional anticoagulation therapies
- Compare and contrast the pharmacokinetics and pharmacodynamics of DOACs and warfarin
- Identify appropriate anticoagulation patients for DOAC therapy
- Apply aspects of the practical management of DOACs to anticoagulation patients in clinical practice

Disclosures

- Potential conflicts of interest: none
Practical Management of DOACs

- Safety and Efficacy Data
- Pharmacokinetics and Pharmacodynamics
- Appropriate Patient Selection
- Dosing
- Laboratory Measurement
- Switching Between Anticoagulants
- Optimizing Transitions of Care

A Shift in Clinical Practice

- 1st class of new oral anticoagulants in over 6 decades
- Represent a shift in the approach to anticoagulation
- Proven to be a safer and more convenient alternative to warfarin
- Prescribing and use is on the rise

Approved Indications

<table>
<thead>
<tr>
<th>Agent</th>
<th>EU</th>
<th>US</th>
<th>Canada</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rivaroxaban (Xarelto)</td>
<td>NVAF Ortho VTE PPX, VTE TX ACS</td>
<td>NVAF Ortho VTE PPX, VTE TX</td>
<td>NVAF Ortho VTE PPX, VTE TX</td>
</tr>
<tr>
<td>Apixaban (Eliquis)</td>
<td>NVAF Ortho VTE PPX VTE TX</td>
<td>NVAF Ortho VTE PPX VTE TX</td>
<td>NVAF Ortho VTE PPX VTE TX</td>
</tr>
<tr>
<td>Dabigatran (Pradaxa)</td>
<td>NVAF Ortho VTE PPX VTE TX</td>
<td>NVAF Ortho VTE PPX VTE TX</td>
<td>NVAF Ortho VTE PPX VTE TX</td>
</tr>
<tr>
<td>Edoxaban (Savaysa)</td>
<td>NVAF VTE TX</td>
<td>NVAF VTE TX</td>
<td>NVAF VTE TX</td>
</tr>
<tr>
<td>Betrixaban (Bevyxxa)</td>
<td>..... VTE PPX</td>
<td>Acute Medical Illness</td>
<td>.....</td>
</tr>
</tbody>
</table>

ACS = acute coronary syndrome; NVAF = non-valvular atrial fibrillation; PPX = prophylaxis; TX = treatment; VTE = venous thromboembolism
DOACs Exceed Warfarin Market Share for New Prescriptions

Current Estimate:
DOACs 70%
Warfarin 30%

Mahan, CE. JTT 2015; DOI 10.1007/s11239-014-1164-4

Practical Management of DOACs

Safety and Efficacy Data
Pharmacokinetics and Pharmacodynamics
Appropriate Patient Selection
Dosing
Laboratory Measurement
Switching Between Anticoagulants
Optimizing Transitions of Care

Acute VTE - Efficacy

As effective as warfarin for preventing recurrent VTE or death
Acute VTE - Safety

Risk of major bleed doubles and risk of ICH triples if warfarin (+LMWH) is used instead of a DOAC for acute VTE.

Acute VTE - Clinical Guidance

- CHEST Guidelines 2016
  - Updated from 2012
  - DOACs preferred over conventional therapy (Grade 2B)

- Anticoagulation Forum VTE Guidance Compendia 2016
  - DOACs suggested as an alternative to conventional therapy in patients who meet appropriate criteria
  - For all other patients, suggest conventional therapy

Conventional therapy = warfarin overlapped with a parenteral anticoagulant


NVAF - Efficacy

20% reduction in stroke/systemic embolism compared to warfarin
Primarily driven by a large reduction in hemorrhagic stroke

**NVAF - Efficacy**

>50% reduction in hemorrhagic stroke compared to warfarin
10% reduction in all-cause mortality compared to warfarin


**NVAF - Safety**

>50% reduction in intracranial hemorrhage
Non-significant trend towards reduction in major bleeding (P=0.06, forest plot not shown)

25% increase in GI bleed
Primarily driven by dabigatran, rivaroxaban, high-dose edoxaban


**NVAF - Clinical Guidance**

<table>
<thead>
<tr>
<th>Guideline</th>
<th>Valvular Disease</th>
<th>CHADS2 = 0</th>
<th>CHADS2 = 1</th>
<th>CHADS2 = 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHEST 2012</td>
<td>Warfarin</td>
<td>No Therapy</td>
<td>Reasonable</td>
<td>OAC</td>
</tr>
<tr>
<td>ACC/AHA/ HRS 2014</td>
<td>CHA2DS2-VASc ≤ 1</td>
<td>No Therapy</td>
<td>Reasonable</td>
<td>OAC</td>
</tr>
<tr>
<td>ESC 2016</td>
<td>Warfarin</td>
<td>No Therapy</td>
<td>Reasonable</td>
<td>OAC</td>
</tr>
</tbody>
</table>

**Guideline**

- **CHEST 2012**: Dabigatran preferred over warfarin (Grade 2B)
- **ACC/AHA/HRS 2014**: Warfarin (Class IA), dabigatran, rivaroxaban, apixaban (Class IIb)
- **ESC 2016**: Warfarin (Class IA), dabigatran, rivaroxaban, apixaban, edoxaban (Class IA)

Practical Management of DOACs

Safety and Efficacy Data
Pharmacokinetics and Pharmacodynamics
Appropriate Patient Selection
Dosing
Laboratory Measurement
Switching Between Anticoagulants
Optimizing Transitions of Care

Mechanisms of Action

Comparison of Oral Anticoagulants

<table>
<thead>
<tr>
<th>Target(s)</th>
<th>Warfarin</th>
<th>Dabigatran</th>
<th>Rivaroxaban</th>
<th>Apixaban</th>
<th>Edoxaban</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak Effect</td>
<td>4.5 days</td>
<td>1.5-3 h</td>
<td>2.4 h</td>
<td>1.3 h</td>
<td>1.2 h</td>
</tr>
<tr>
<td>Half-Life</td>
<td>40 h</td>
<td>12-17 h</td>
<td>5-9 h</td>
<td>9-14 h</td>
<td>10-14 h</td>
</tr>
<tr>
<td>Renal Elimination</td>
<td>None</td>
<td>80%</td>
<td>33%</td>
<td>25%</td>
<td>35-50%</td>
</tr>
<tr>
<td>Dialyzable</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Possible</td>
</tr>
<tr>
<td>Interactions</td>
<td>Many</td>
<td>P-gp</td>
<td>3A4, P-gp</td>
<td>3A4, P-gp</td>
<td>P-gp</td>
</tr>
<tr>
<td>Coagulation Monitoring</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Antidote</td>
<td>Vitamin K</td>
<td>Idarucizumab</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Lab Measure</td>
<td>INR</td>
<td>aPTT</td>
<td>TT, dTT, ECT</td>
<td>PT</td>
<td>Anti-Xa</td>
</tr>
</tbody>
</table>
Pros and Cons
DOACs Compared to Warfarin

Pros
- Rapid onset of action
- Short half-lives
- Predictable pharmacokinetics
- Fewer drug interactions
- Lack of need for routine monitoring of anticoagulant activity
- Improved safety, equal efficacy
- May be cost effective at health system level

Cons
- Requires high-degree of adherence
- Drug accumulation with renal impairment
- No reliable, clinically available test to determine levels
- No specific antidotes to reverse anticoagulant effect
- Fewer studies and/or approved indications
- Cost prohibitive at patient level

Practical Management of DOACs

Safety and Efficacy Data
Pharmacokinetics and Pharmacodynamics
Appropriate Patient Selection
Dosing
Laboratory Measurement
Switching Between Anticoagulants
Optimizing Transitions of Care

DOAC Considerations

- Adherence
- Renal Function
- Concomitant Medications
- Altered Exposure to DOAC
- Age
- Weight
Case 1

Which of the following patients would be considered a good candidate for DOAC therapy?

A. 54-year-old male with a history of recurrent VTE and labile INR due to non-compliance with warfarin therapy
B. 37-year-old female with end-stage renal disease, on hemodialysis, who has thrombosed her dialysis fistula
C. 64-year-old male with a St. Jude’s mechanical mitral valve admitted for atrial fibrillation with RVR
D. 65-year-old female with diabetes & hypertension (both well-controlled with medication), normal kidney function and new onset non-valvular atrial fibrillation

Adherence to Therapy

<table>
<thead>
<tr>
<th>Renal Effect</th>
<th>Dabigatran</th>
<th>Rivaroxaban</th>
<th>Apixaban</th>
<th>Edoxaban</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renal Clearance</td>
<td>80%</td>
<td>33%</td>
<td>25%</td>
<td>50%</td>
</tr>
<tr>
<td>t½ CrCl &gt; 60 mL/min</td>
<td>14 h</td>
<td>8.5 h</td>
<td>15.1 h</td>
<td>8.6 h</td>
</tr>
<tr>
<td>t½ CrCl 30–60 mL/min</td>
<td>18.7 h</td>
<td>9.0 h</td>
<td>17.6 h</td>
<td>9.4 h</td>
</tr>
<tr>
<td>t½ CrCl 15–30 mL/min</td>
<td>27.5 h</td>
<td>9.5 h</td>
<td>17.3 h</td>
<td>16.9 h</td>
</tr>
</tbody>
</table>

ESRD and Dialysis

- FDA labeling
  - Apixaban: may be used in NVAF patients with ESRD
  - Rivaroxaban: suggests the same as apixaban, but does not have FDA-approval in that population
- Patients with severe renal impairment (CrCl 15-30 ml/min) or undergoing hemodialysis (CrCl <15 ml/min) were excluded from all DOAC clinical trials
- Dosing recommendations are based on pharmacokinetic and pharmacodynamic data only
  - Single-dose trials (no evaluation of drug accumulation)
  - Very small sample size (n=8 in active arms)

Avoid All DOACs in Severe Renal Impairment and Hemodialysis Until More Data Becomes Available

DOAC Drug Interactions*

Dabigatran & Edoxaban
- Avoid concomitant use with strong inhibitors/inducers of P-gp
- Avoid concomitant use with combined strong inhibitors/inducers of P-gp and CYP 3A4

Apixaban & Rivaroxaban
- Avoid concomitant use with DOAC unless benefit clearly justifies increased bleed risk

Concomitant Antiplatelets and NSAIDs
- Avoid concomitant use with DOAC unless benefit clearly justifies increased bleed risk

* lists are not exhaustive

How Should DOAC Interactions Be Managed?

Dabigatran and Edoxaban
- Avoid concomitant use with strong inhibitors/inducers of P-gp

Rivaroxaban and Apixaban
- Avoid concomitant use with combined strong inhibitors/inducers of P-gp and CYP 3A4

Concomitant Antiplatelets and NSAIDs
- Avoid concomitant use with DOAC unless benefit clearly justifies increased bleed risk

DOAC Therapy and Mechanical Valves

- RE-ALIGN Trial
  - 252 patients with AVR or MVR
  - Valve replacement within the past 7 days
  - Valve replacement ≥ 3 months
  - Warfarin vs. dabigatran (150mg BID, 220mg BID, 300mg BID)

  **↑ Stroke: 0% warfarin vs. 5% dabigatran**
  **↑ Major Bleeding: 2% warfarin vs. 4% dabigatran**

TERMINATED EARLY

---

DOAC Therapy and VTE + Active Cancer (CA)

- DOAC VTE treatment RCTs included few CA patients
- Meta-analyses suggest DOACs = warfarin for VTE in CA patients
- Unknown if DOACs = LMWH
- Ongoing clinical trials should provide more guidance
- DOACs not currently recommended as 1st line in CA + VTE
- LMWH monotherapy remains preferred

Percentage of Subjects with Cancer

<table>
<thead>
<tr>
<th>Study</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMPLIFY-EXT</td>
<td>1.8</td>
</tr>
<tr>
<td>EINSTEIN-EXT</td>
<td>4.7</td>
</tr>
<tr>
<td>EINSTEIN-PE</td>
<td>4.7</td>
</tr>
<tr>
<td>EINSTEIN-DVT</td>
<td>6.8</td>
</tr>
<tr>
<td>RE-COVER</td>
<td>5.0</td>
</tr>
<tr>
<td>HOKUSAI</td>
<td>9.2</td>
</tr>
</tbody>
</table>

---

DOAC Therapy and Other Patient Populations

- Suggest avoiding DOAC therapy for VTE with the following:
  - Antiphospholipid antibody syndrome
  - Extremes of weight (<50kg or >120kg)
- Lack of available data
DOAC Patient Selection Criteria

- Indication for anticoagulation that has been adequately studied and approved with DOACs
- No need for advanced or invasive therapies
- No contraindications (pregnant, breastfeeding, mech. valve)
- Adequate organ function
  - Avoid in severe renal impairment
  - Avoid in moderate to severe hepatic impairment
- Lack of significant drug interactions
- Highly likely to adhere to therapy
- Confirmed ability to obtain DOAC longitudinally

Practical Management of DOACs

Safety and Efficacy Data
Pharmacokinetics and Pharmacodynamics
Appropriate Patient Selection
Dosing
Laboratory Measurement
Switching Between Anticoagulants
Optimizing Transitions of Care

Case 2

- 34 yo M presents to the emergency department with a femoral DVT likely due to a recent surgery
- He is otherwise healthy and clinically stable
- Which of the following anticoagulation regimens would be preferred for initial VTE treatment in this patient?

A. IV unfractionated heparin overlapped with warfarin
B. Low molecular weight heparin monotherapy
C. Dabigatran 150 mg PO BID
D. Rivaroxaban 15 mg PO BID
DOAC Initiation for Acute VTE

Conventional VTE Treatment

<table>
<thead>
<tr>
<th>Drug</th>
<th>Indication</th>
<th>U.S. Labeled Dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dabigatran</td>
<td>VTE Treatment</td>
<td>CrCl &gt; 30 mL/min: 150 mg BID*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CrCl &lt; 30 mL/min: Avoid Use</td>
</tr>
<tr>
<td></td>
<td>Non-Valvular Atrial Fibrillation</td>
<td>CrCl &gt; 30 mL/min: 150 mg BID</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CrCl 15–30 mL/min: 75 mg BID</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CrCl &lt; 15 mL/min: Avoid Use</td>
</tr>
<tr>
<td>Rivaroxaban</td>
<td>VTE Treatment</td>
<td>15 mg BID x 21 days; then 20 mg daily</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CrCl &lt; 30 mL/min: Avoid Use</td>
</tr>
<tr>
<td></td>
<td>Non-Valvular Atrial Fibrillation</td>
<td>CrCl &gt; 50 mL/min: 20 mg daily</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CrCl 15–50 mL/min: 15 mg daily</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CrCl &lt; 15 mL/min: Avoid Use</td>
</tr>
</tbody>
</table>

Therapeutic Dosing

- Varies by:
  - DOAC
  - Indication
  - Country
- May require adjustment for:
  - Renal function
  - Age
  - Weight
  - Drug interactions
  - Combination of above

Avoid empiric dose adjustments as this may lead to increased adverse events.

*Dr. UFH or fondaparinux

Therapeutic Dosing for Acute VTE

- Conventional VTE Treatment
- Dabigatran Edoxaban
- Rivaroxaban Apixaban
### Therapeutic Dosing

<table>
<thead>
<tr>
<th>Drug</th>
<th>Indication</th>
<th>U.S. Labeled Dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apixaban</td>
<td>VTE Treatment</td>
<td>10 mg BID x 7 days; then 5 mg BID</td>
</tr>
<tr>
<td></td>
<td>Non-Valvular Atrial Fibrillation</td>
<td>5 mg BID; 2.5 mg BID (if ≥ 2 of the following: ≥ 80 yr, wt ≤ 60 kg, SD ≥ 1.5 kg/dL)</td>
</tr>
<tr>
<td></td>
<td>CrCl &lt; 25 mL/min not studied. Avoid Use.</td>
<td></td>
</tr>
<tr>
<td>Edoxaban</td>
<td>VTE Treatment</td>
<td>60 mg daily*</td>
</tr>
<tr>
<td></td>
<td>Non-Valvular Atrial Fibrillation</td>
<td>60 mg daily (if CrCL &gt; 50 mL/min; CrCl 15-50 mL/min: 30 mg daily)</td>
</tr>
<tr>
<td></td>
<td>CrCl &gt; 50 mL/min: Do Not Use</td>
<td></td>
</tr>
<tr>
<td></td>
<td>CrCl &gt; 95 mL/min: Do Not Use</td>
<td></td>
</tr>
<tr>
<td></td>
<td>CrCl &lt; 15 mL/min: Avoid Use</td>
<td></td>
</tr>
</tbody>
</table>

*5-day parenteral lead-in then switch to DOAC

Savaysa (edoxaban) [package insert]. Daiichi Sankyo. 2015

---

### Practical Management of DOACs

- **Safety and Efficacy Data**
- **Pharmacokinetics and Pharmacodynamics**
- **Appropriate Patient Selection**
- **Dosing**
- **Laboratory Measurement**
- **Switching Between Anticoagulants**
- **Optimizing Transitions of Care**

---

### Measurement of DOACs

- Increased specificity for target inhibition
- Predictable pharmacokinetic and pharmacodynamic response
- Minimal dietary effect
- Less intrasubject and intersubject variability
- Wide therapeutic index
- Do not require routine monitoring
  - Dose is not adjusted based on laboratory measurements
  - No quantitative “therapeutic ranges” established
Measurement of DOACs

<table>
<thead>
<tr>
<th>Potential Indications for DOAC Measurement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Detection of Clinically Relevant Levels</td>
</tr>
<tr>
<td>Urgent or emergent invasive procedure</td>
</tr>
<tr>
<td>Neuraxial anesthesia</td>
</tr>
<tr>
<td>Major trauma</td>
</tr>
<tr>
<td>Potential thrombolysis in acute thromboembolism</td>
</tr>
<tr>
<td>Hemorrhage</td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>

Measurement of DOACs

Suggestions for laboratory measurement of DOACs

- If measurement is indicated
  - Use assays that are validated locally or in a reference laboratory
  - Use assays that are readily available
  - Chosen assay must be suitable for the prescribed DOAC
  - Chosen assay must be suitable for the indication for measurement

<table>
<thead>
<tr>
<th>Drug</th>
<th>Suggested Test TT</th>
<th>Interpretation</th>
<th>Suggested Test aPTT/ Dilute TT, ECA, ECT</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dabigatran</td>
<td>Normal TT likely excludes clinically relevant drug levels</td>
<td>Dabigatran TT, ECA, ECT</td>
<td>Normal TT likely excludes clinically relevant drug levels</td>
<td>Dabigatran TT, ECA, ECT</td>
</tr>
<tr>
<td>Rivaroxaban</td>
<td>Normal anti-Xa activity likely excludes clinically relevant drug levels</td>
<td>Anti-Xa</td>
<td>Normal anti-Xa activity likely excludes clinically relevant drug levels</td>
<td>Anti-Xa</td>
</tr>
<tr>
<td>Apixaban</td>
<td>Normal anti-Xa activity likely excludes clinically relevant drug levels</td>
<td>Anti-Xa</td>
<td>Normal anti-Xa activity likely excludes clinically relevant drug levels</td>
<td>Anti-Xa</td>
</tr>
<tr>
<td>Edoxaban</td>
<td>Normal anti-Xa activity likely excludes clinically relevant drug levels</td>
<td>Anti-Xa</td>
<td>Normal anti-Xa activity likely excludes clinically relevant drug levels</td>
<td>Anti-Xa</td>
</tr>
</tbody>
</table>

How Should DOACs Be Measured?

Suggestions for laboratory measurement of DOACs

- Normal TT likely excludes clinically relevant drug levels
- Normal aPTT likely excludes clinically relevant drug levels
- Only dilute TT, ECA, and ECT are suitable for quantitation
Practical Management of DOACs

<table>
<thead>
<tr>
<th>Safety and Efficacy Data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pharmacokinetics and Pharmacodynamics</td>
</tr>
<tr>
<td>Appropriate Patient Selection</td>
</tr>
<tr>
<td>Dosing</td>
</tr>
<tr>
<td>Laboratory Measurement</td>
</tr>
<tr>
<td>Switching Between Anticoagulants</td>
</tr>
<tr>
<td>Optimizing Transitions of Care</td>
</tr>
</tbody>
</table>

Case 3

- 64 yo F admitted from rehab for massive PE with some right heart strain
- Recent bilateral total knee arthroplasties, on LMWH for VTE prophylaxis and reports good adherence
- IV UFH infusion started. It is decided to not employ thrombolytics.

Which of the following would be the safest, most evidenced-based approach regarding switching her to longer-term anticoagulation therapy?

A. Initiate dabigatran and overlap with IV UFH for 5 days
B. Stop the IV UFH and start dabigatran or edoxaban alone now
C. Stop the IV UFH and start rivaroxaban or apixaban alone now
D. Stop the IV UFH and start rivaroxaban in 6-8 hours

Switching Between Anticoagulants

- Can place patients at undue risk for adverse events
  - e.g., bleeding or thrombosis

- Requires a “carefully constructed and thoughtful approach”

- Should be based on:
  - Pharmacokinetic profile of each anticoagulant
  - Appropriate laboratory assessment of patient’s coagulation status
  - Patient’s renal function

Switching Between Anticoagulants

- Unfractionated heparin
  - Short half-life precludes need for lag time until alternative anticoagulant is initiated

- DOACs and SQ injectables (LMWH, fondaparinux)
  - Longer half-life requires lag time until alternative anticoagulant is initiated

- Warfarin
  - From: Extremely long half-life requires confirmed offset via INR
  - To: Slow onset may require overlap of rapid-acting anticoagulant

Switching to a DOAC

<table>
<thead>
<tr>
<th>Agent to DOAC</th>
<th>Strategy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warfarin to DOAC</td>
<td>Stop warfarin</td>
</tr>
<tr>
<td></td>
<td>Start DOAC when INR &lt; 2.5 and trending downward</td>
</tr>
<tr>
<td>LMWH (or DOAC) to DOAC</td>
<td>Start DOAC within 0-2 hours of next dose of LMWH (or DOAC)</td>
</tr>
<tr>
<td>IV heparin to DOAC</td>
<td>Start DOAC within 30 minutes after stopping IV heparin</td>
</tr>
</tbody>
</table>

Switching to Warfarin

<table>
<thead>
<tr>
<th>DOAC</th>
<th>Strategy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dabigatran</td>
<td>Start warfarin and overlap dabigatran based on renal function</td>
</tr>
<tr>
<td></td>
<td>CrCl ≥ 90 mL/min: overlap 3 days</td>
</tr>
<tr>
<td></td>
<td>CrCl 30-90 mL/min: overlap 2 days</td>
</tr>
<tr>
<td>Rivaroxaban</td>
<td>Stop DOAC</td>
</tr>
<tr>
<td>Apixaban</td>
<td>Start warfarin and LMWH at time of next scheduled DOAC dose and bridge until INR ≥ 2.0</td>
</tr>
<tr>
<td>Edoxaban</td>
<td>60 mg dose: reduce dose to 30 mg and start warfarin concomitantly</td>
</tr>
<tr>
<td></td>
<td>30 mg dose: reduce dose to 15 mg and start warfarin concomitantly</td>
</tr>
<tr>
<td></td>
<td>Stop edoxaban when INR ≥ 2.0</td>
</tr>
</tbody>
</table>

Either strategy may be employed – If DOAC is chosen to overlap warfarin, measure INR just before next DOAC dose
Case 4

- 63 yo M with acute popliteal DVT expresses preference for treatment with rivaroxaban. Which of the following is the most appropriate follow-up strategy for this patient?

A. A follow-up appointment should be scheduled for 3 days after discharge to check his rivaroxaban level

B. He should be scheduled for follow-up within the first 2 weeks of discharge to ensure appropriate dose de-escalation of his rivaroxaban

C. He should be scheduled for follow-up 5 days after discharge to stop his parental agent and switch to rivaroxaban

D. He does not require any kind of routine follow-up, as the DOACs do not require monitoring

Transitions of Care

- Incorporate key anticoagulation information into EHR documentation (e.g., indication, intended duration)

- Evaluate all VTE patients for outpatient treatment

- Use a DOAC discharge checklist
  - DOAC education to patient and caregivers
  - Safety net phone number provided
  - If transferred to another facility, ensure DOAC on formulary
  - Documented time of last and next dose of DOAC
  - Referral to appropriate provider
  - For VTE: prescribed strategy for switch to DOAC from parenteral or dose de-escalation at specified time
Outpatient Follow Up

- Initial follow up interval every 1-3 months
- May eventually be extended to every 6-12 months
- No routine monitoring of anticoagulant activity
- Monitor renal function consistently
- Monitor CBC, liver function tests periodically
- Discuss key questions
  - What medications have you stopped/started?
  - What kidney/liver problems have you had?
  - What side effects have you had from your medication?
  - What problems have you had getting your DOAC filled?
  - What extra or missed doses have you had?
  - What upcoming surgical or dental procedures do you have?
  - What medical procedures or hospitalizations have you had?
  - What is the possibility of stopping anticoagulation?

Conclusions

DOACs have rapidly expanded VTE treatment options and are now preferred over conventional therapies for convenience and safety reasons

Specific segments of the population are not DOAC candidates and appropriate patient selection is imperative

Although a significant advance in anticoagulation, DOACs demand expertise from the prescribing clinicians and effective patient education to ensure optimal outcomes for patients

Guidelines for the practical management of the direct oral anticoagulants (DOACs) in VTE treatment

- Free access online
- On-demand webinar available at www.acforum.org
Thank You!
Questions?