Direct Oral Anticoagulants as an Alternative to Warfarin Therapy in Oncology Patients

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Chelsea Manion, PharmD, BCPS
Disclosures

Cindy Brucato
• I have nothing to disclose concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation

Chelsea Manion
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RPh Objectives

• Review the pathophysiology and risk of thrombosis in oncology patients

• Evaluate recent literature regarding use of direct oral anticoagulants for treatment of thrombosis in oncology patients

• Discuss possible unique drug interactions between direct oral anticoagulants and chemotherapy agents

• Apply literature to specific oncology patient cases in clinical practice
CPhT Objectives

• Discuss rationale for increased risk of thrombosis in oncology patients
• Identify the medications in the class of direct oral anticoagulant
• Describe common concerns for the use of anticoagulants in the oncology patient population
Abbreviations

DOAC → direct oral anticoagulant
AC → anticoagulant
OAC → oral anticoagulant
LMWH → low molecular weight heparin
UFH → unfractionated heparin
VTE → venous thromboembolism
DVT → deep vein thrombosis
PE → pulmonary embolism
CA → cancer
5-FU → 5-fluorouracil

INR → International normalized ratio
CrCl → creatinine clearance
sCr → serum creatinine
Wt → weight
CKD → chronic kidney disease
CRNMB → clinically relevant non-major bleeding
TTR → time in therapeutic range
P-gp → P glycoprotein
EGOG → Eastern Cooperative Oncology Group
Who are we & who are you?
VTE in Cancer
Epidemiology

Represent 15-20% of the diagnosed VTE

8-19% incidence dependent on tumor type
  ◦ Versus 1.4% in a gender-matched cohort

3-fold higher risk of recurrent VTE on and off anticoagulation (AC)
  ◦ Metastatic vs. localized
  ◦ 10-20% recurrence rate after the full duration of AC

10% of idiopathic VTE lead to diagnosis of cancer within 1 year

Increase risk of death
Pathophysiology

Hypercoagulability  Vessel damage  Stasis

Inflammation

Cancer-Associated Venous Thromboembolic Disease Version 1.2015
Risk Factors

Not all risk factors are associated with the underlying cancer

Tumor type
- Brain (30%)
- Pancreas
- Adenocarcinoma > squamous
- Metastatic vs. localized

Other considerations
- Bleeding
- Chemotherapy
  - i.e. thalidomide & lenalidomide
- Hormonal therapy
- Indwelling catheters
- NVD

Increased risk of bleeding

Cancer-Associated Venous Thromboembolic Disease Version 1.2015
Jo JT. Semin Thromb Hemost 2014;40:352-331
Clinical Considerations

CONTRAINDICATIONS TO PROPHYLACTIC OR THERAPEUTIC ANTICOAGULATION TREATMENT

**Absolute**
- Recent central nervous system (CNS) bleed, intracranial or spinal lesion at high risk for bleeding
- Active bleeding (major): more than 2 units transfused in 24 hours

**Relative**
- Chronic, clinically significant measurable bleeding >48 hours
- Thrombocytopenia (platelets <50,000/mcL)
- Severe platelet dysfunction (uremia, medications, dysplastic hematopoiesis)
- Recent major operation at high risk for bleeding
- Underlying hemorrhagic coagulopathy
- High risk for falls (head trauma)
- Neuraxial anesthesia/lumbar puncture

CONTRAINDICATIONS TO MECHANICAL PROPHYLAXIS

**Absolute**
- Acute DVT
- Severe arterial insufficiency (pertains to GCS only)

**Relative**
- Large hemoma
- Skin ulcerations or wounds
- Thrombocytopenia (platelets <20,000/mcL) or petechiae
- Mild arterial insufficiency (pertains to GCS only)
- Peripheral neuropathy (pertains to GCS only)
## ECOG Performance Status*


<table>
<thead>
<tr>
<th>Grade</th>
<th>ECOG</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No restrictions in ADLs</td>
</tr>
<tr>
<td>1</td>
<td>ADLs intact, able to carry out physically light work, able to work in moderation</td>
</tr>
<tr>
<td>2</td>
<td>50% of the time up and moving, ADLs intact, unable to work</td>
</tr>
<tr>
<td>3</td>
<td>50% of the time confined to bed or chair, severe limitations in ADLs</td>
</tr>
<tr>
<td>4</td>
<td>Confined to bed or chair at all times</td>
</tr>
<tr>
<td>5</td>
<td>Dead</td>
</tr>
</tbody>
</table>
Clinical Considerations

Prophylaxis
- Hospitalized patients without contraindications
- MM patients with thalidomide or lenalidomide treatment
- Routine use in the absence of risk factors is not recommended
- Surgical patients, recommended outpatient for up to 4 weeks for high-risk surgeries

Treatment
- Ongoing with active cancer
  - Metastatic cancer
  - Treatment goals

Recurrent VTE
- Data supports switching to LMWH if not already on, optimizing dosing if already on, or IVC filter
CLOT Trial

LMWH vs. VKA in VTE with cancer

338 patients in each arm
  • Breast, colon, lung, GU, gyne, pancreatic, brain, and other cancers

Primary outcome was recurrent VTE
  • 0.48 (0.3-0.77, 95%, p=0.002) in favor of dalteparin

Secondary outcome was safety
  • Bleeding: 19/335 in dalteparin vs. 12/335 in warfarin p=0.27
  • Mortality: 130 in dalteparin vs. 136 in warfarin p=0.53

Of note, excluded patients with ECOG > 3 and not a great sample of hematologic malignancies

Lee AYY. NEJM 2003;349:146-153
Agents and Evidence
CHEST VTE Guidelines 2016

In patients with DVT or PE and cancer (“cancer-associated thrombosis”), as long-term (first 3 months) anticoagulant therapy, we suggest LMWH over VKA (Grade 2C), dabigatran (Grade 2C), rivaroxaban (Grade 2C), apixaban (Grade 2C), or edoxaban (Grade 2C)

LMWH → VKA = DOACs

In patients with DVT or PE and cancer (“cancer-associated thrombosis”), and who (i) do not have a high bleeding risk, we recommend extended anticoagulation therapy (no scheduled stop date) over 3 months of therapy (Grade 1B), or (ii) have a high risk of bleeding, we suggest extended anticoagulant therapy (no scheduled stop date over 3 months of therapy (Grade 2B)

NCCN Guidelines 2015

Recommend LMWH over VKA

Not enough evidence to support the use of DOACs in cancer patients
American Society of Clinical Oncology Guidelines 2014

• LMWH is preferred over UFH for the initial 5 to 10 days of anticoagulation for the cancer patient with newly diagnosed VTE who does not have severe renal impairment (defined as creatinine clearance < 30 mL/min).

• For long-term anticoagulation, LMWH for at least 6 months is preferred due to improved efficacy over Vitamin K antagonists.
  • Vitamin K antagonists are an acceptable alternative for long-term therapy if LMWH is not available.

• Anticoagulation with LMWH or Vitamin K antagonist beyond the initial 6 months may be considered for select patients with active cancer, such as those with metastatic disease or those receiving chemotherapy.

• Use of novel oral anticoagulants for either prevention or treatment of VTE in cancer patients is not recommended at this time.

LMWH → VKA  ≠  DOAC

Lyman GH. J Clin Oncol. 2015;33:654-656.
DOACS

- Direct Thrombin Inhibitor
  - Dabigatran

- Direct Factor Xa Inhibitor
  - Rivaroxaban
    - Apixaban
    - Edoxaban
## Dabigatran vs. VKA

### Pooled results from RECOVER I and II Trials

<table>
<thead>
<tr>
<th></th>
<th>Dabigatran</th>
<th>VKA</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dose</strong></td>
<td>5-10 days of LWMH then dabigatran 150mg BID</td>
<td>LMWH bridge then dose adjusted VKA based on INR</td>
</tr>
<tr>
<td><strong>Patients (n)</strong></td>
<td>173</td>
<td>162</td>
</tr>
<tr>
<td><strong>Recurrent VTE or VTE related death</strong></td>
<td>10 (5.8%)</td>
<td>12 (7.4%)</td>
</tr>
<tr>
<td><strong>Major bleed</strong></td>
<td>6 (3.8%)</td>
<td>7 (4.6%)</td>
</tr>
<tr>
<td><strong>Any bleed</strong></td>
<td>39 (24.5%)</td>
<td>(35 (23%))</td>
</tr>
</tbody>
</table>

## Dosing for DOACS for Treatment of VTE

<table>
<thead>
<tr>
<th></th>
<th>CLOT</th>
<th>Rivaroxaban EINSTEIN DVT &amp; PE</th>
<th>Apixaban AMPLIFY</th>
<th>Edoxaban HOKUSAI VTE</th>
</tr>
</thead>
<tbody>
<tr>
<td>AC #1</td>
<td>Dalteparin 200 IU/kg/day</td>
<td>Rivaroxaban 15mg BID x21 days then 20mg daily</td>
<td>Apixaban 10mg BID x7 days then 5mg BID</td>
<td>Edoxaban 60mg daily</td>
</tr>
<tr>
<td>AC #2</td>
<td>Dose adjusted VKA</td>
<td>Dose adjusted VKA</td>
<td>Dose adjusted VKA</td>
<td>Dose adjusted VKA</td>
</tr>
<tr>
<td>Was parenteral agent required before OAC #1</td>
<td>N/A</td>
<td>No</td>
<td>No</td>
<td>Yes Median 7 days</td>
</tr>
</tbody>
</table>

Lee AYY. NEJM 2003;349:146-153.  
## Active Cancer data for DOAC Trials

<table>
<thead>
<tr>
<th>Anticoagulation</th>
<th>CLOT</th>
<th>Rivaroxaban</th>
<th>EINSTEIN DVT &amp; PE</th>
<th>Apixaban</th>
<th>AMPLIFY</th>
<th>Edoxaban</th>
<th>HOKUSAI VTE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anticoagulation</td>
<td>LMWH</td>
<td>VKA</td>
<td>DOAC</td>
<td>VKA</td>
<td>DOAC</td>
<td>VKA</td>
<td>DOAC</td>
</tr>
<tr>
<td>Patients (n)</td>
<td>338</td>
<td>338</td>
<td>258</td>
<td>204</td>
<td>88</td>
<td>81</td>
<td>109</td>
</tr>
<tr>
<td>Mean age (yr)</td>
<td>62</td>
<td>63</td>
<td>NR</td>
<td>NR</td>
<td>65.5</td>
<td>65.1</td>
<td>NR</td>
</tr>
<tr>
<td>Male gender</td>
<td>47%</td>
<td>50%</td>
<td>59%</td>
<td>53%</td>
<td>56.8%</td>
<td>60.5%</td>
<td>NR</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>79.19</td>
<td>81.69</td>
<td>NR</td>
</tr>
<tr>
<td>CrCl 30-50ml/min</td>
<td>NR</td>
<td>NR</td>
<td>13%</td>
<td>17%</td>
<td>8%</td>
<td>13.6%</td>
<td>NR</td>
</tr>
<tr>
<td>CrCl &lt;30ml/min</td>
<td>NR</td>
<td>NR</td>
<td>0%</td>
<td>0%</td>
<td>3.4%</td>
<td>1.2%</td>
<td>NR</td>
</tr>
<tr>
<td>TTR</td>
<td>N/A</td>
<td>46%</td>
<td>N/A</td>
<td>57%</td>
<td>N/A</td>
<td>57.5%</td>
<td>N/A</td>
</tr>
</tbody>
</table>

# History of Cancer data for DOAC Trials

<table>
<thead>
<tr>
<th></th>
<th>CLOT</th>
<th>Rivaroxaban EINSTEIN DVT &amp; PE</th>
<th>Apixaban AMPLIFY</th>
<th>Edoxaban HOKUSAI VTE</th>
</tr>
</thead>
<tbody>
<tr>
<td>** Anticoagulation **</td>
<td>LMWH</td>
<td>VKA</td>
<td>DOAC</td>
<td>VKA</td>
</tr>
<tr>
<td>Patients (n)</td>
<td>N/A</td>
<td>N/A</td>
<td>233</td>
<td>236</td>
</tr>
<tr>
<td>Mean age (yr)</td>
<td>N/A</td>
<td>N/A</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Male gender</td>
<td>N/A</td>
<td>N/A</td>
<td>52%</td>
<td>52%</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>N/A</td>
<td>N/A</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>CrCl 30-50ml/min</td>
<td>N/A</td>
<td>N/A</td>
<td>18%</td>
<td>13%</td>
</tr>
<tr>
<td>CrCl &lt;30ml/min</td>
<td>N/A</td>
<td>N/A</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>TTR</td>
<td>N/A</td>
<td>N/A</td>
<td>63%</td>
<td>64.5%</td>
</tr>
</tbody>
</table>

# Types of cancer included

<table>
<thead>
<tr>
<th>Type</th>
<th>CLOT</th>
<th>Rivaroxaban EINSTEIN DVT &amp; PE</th>
<th>Apixaban AMPLIFY</th>
<th>Edoxaban HOKUSAI VTE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active Cancer</td>
<td>676 (100%)</td>
<td>462 (5.6%)</td>
<td>169 (3.1%)</td>
<td>208 (2.5%)</td>
</tr>
<tr>
<td>History of Cancer</td>
<td>N/A</td>
<td>469 (5.7%)</td>
<td>365 (6.8%)</td>
<td>563 (6.8%)</td>
</tr>
<tr>
<td>Total</td>
<td>676 (100%)</td>
<td>931 (11.2%)</td>
<td>534 (9.9%)</td>
<td>771 (9.3%)</td>
</tr>
<tr>
<td>Breast</td>
<td>108 (16%)</td>
<td>53 (11.5%)</td>
<td>79 (14.8%)</td>
<td>NR</td>
</tr>
<tr>
<td>Colon</td>
<td>108 (16%)</td>
<td>44 (9.5%)</td>
<td>67 (12.5%)</td>
<td>NR</td>
</tr>
<tr>
<td>Lung</td>
<td>90 (13.3%)</td>
<td>34 (7.6%)</td>
<td>43 (8%)</td>
<td>NR</td>
</tr>
<tr>
<td>Genitourinary tract</td>
<td>86 (12.7%)</td>
<td>143 (31%)</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Prostate</td>
<td>NR</td>
<td>NR</td>
<td>85 (15.9%)</td>
<td>NR</td>
</tr>
<tr>
<td>Bladder</td>
<td>NR</td>
<td>NR</td>
<td>43 (8%)</td>
<td>NR</td>
</tr>
<tr>
<td>Metastatic</td>
<td>455 (67.3%)</td>
<td>101 (21.9%)</td>
<td>176 (33%)</td>
<td>NR</td>
</tr>
<tr>
<td>Diagnosed with CA during trial</td>
<td>N/A</td>
<td>193</td>
<td>25</td>
<td>NR</td>
</tr>
</tbody>
</table>
### Efficacy Results in Oncology Patients

<table>
<thead>
<tr>
<th>Anticoagulant</th>
<th>CLOT</th>
<th>Rivaroxaban EINSTEIN DVT &amp; PE</th>
<th>Apixaban AMPLIFY</th>
<th>Edoxaban HOKUSAI VTE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>LMWH</td>
<td>VKA</td>
<td>DOAC</td>
<td>VKA</td>
</tr>
<tr>
<td>Recurrent VTE with active CA</td>
<td>27 (8%)</td>
<td>53 (16%)</td>
<td>6 (2%)</td>
<td>8 (4%)</td>
</tr>
<tr>
<td>Recurrent VTE with h/o CA</td>
<td>N/A</td>
<td>N/A</td>
<td>5 (2%)</td>
<td>5 (2%)</td>
</tr>
<tr>
<td>Recurrent VTE with active CA or h/o CA</td>
<td>N/A</td>
<td>N/A</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Mortality with active CA</td>
<td>130 (39%)</td>
<td>136 (41%)</td>
<td>38 (15%)</td>
<td>36 (18%)</td>
</tr>
<tr>
<td>Mortality with h/o CA</td>
<td>N/A</td>
<td>N/A</td>
<td>5 (2%)</td>
<td>4 (2%)</td>
</tr>
</tbody>
</table>

# Safety Results in Oncology Patients

<table>
<thead>
<tr>
<th></th>
<th>CLOT</th>
<th>Rivaroxaban EINSTEIN DVT &amp; PE</th>
<th>Apixaban AMPLIFY</th>
<th>Edoxaban HOKUSAI VTE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anticoagulant</td>
<td>LMWH</td>
<td>VKA</td>
<td>DOAC</td>
<td>VKA</td>
</tr>
<tr>
<td>Major bleed with active CA</td>
<td>19 (6%)</td>
<td>12 (4%)</td>
<td>5 (2%)</td>
<td>8 (4%)</td>
</tr>
<tr>
<td>CRNMB with active CA</td>
<td>NR</td>
<td>NR</td>
<td>30 (12%)</td>
<td>27 (13%)</td>
</tr>
<tr>
<td>Composite bleed with active CA</td>
<td>47 (14%)</td>
<td>64 (19%)</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Major bleed with h/o CA</td>
<td>N/A</td>
<td>N/A</td>
<td>1 (&lt;1%)</td>
<td>4 (2%)</td>
</tr>
<tr>
<td>CRNMB with h/o CA</td>
<td>N/A</td>
<td>N/A</td>
<td>25 (11%)</td>
<td>22 (9%)</td>
</tr>
<tr>
<td>Composite bleed with h/o CA</td>
<td>N/A</td>
<td>N/A</td>
<td>NR</td>
<td>NR</td>
</tr>
</tbody>
</table>

Ongoing DOAC Trials in Oncology Patients

**Rivaroxaban in the treatment of venous thromboembolism (VTE) in Cancer Patients**

- **Inclusion Criteria**
  - Newly diagnosed with acute VTE
  - Active malignancy
  - Life expectancy ≥ 6 months
  - Platelets ≥ 100,000/μL, INR < 1.5, and PTT < 40 seconds

- **Exclusion Criteria**
  - CrCl < 30 ml/min
  - Treatment with another therapeutic anticoagulant for > 96 hours prior to study treatment
  - Acute clinically relevant bleeding in the last 2 weeks
  - History of spontaneous major or cerebral bleeding
  - Liver disease (including Child B and C) or cirrhosis
  - Acute medical illness
  - Known conditions associated with high risk of bleeding, known history of hemorrhagic diathesis

- **Primary Outcome**
  - Patient reported treatment satisfaction (convenience) with rivaroxaban vs. LMWH

<table>
<thead>
<tr>
<th>AC #1</th>
<th>Rivaroxaban 15mg BID x21 days then 20mg daily</th>
</tr>
</thead>
<tbody>
<tr>
<td>AC #2</td>
<td>Enoxaparin 1mg/kg BID, Tinzaparin 175 IU/kg daily, or dalteparin 200 IU/kg daily</td>
</tr>
<tr>
<td>Was parenteral agent required before OAC #1</td>
<td>No</td>
</tr>
</tbody>
</table>
Ongoing DOAC Trials in Oncology Patients

• **Hokusai – VTE Cancer Trial**

<table>
<thead>
<tr>
<th>Inclusion Criteria</th>
<th>Exclusion Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active CA or diagnosed within 2 years prior to randomization (other than basal cell or squamous cell carcinoma)</td>
<td>CrCl &lt; 30 ml/min</td>
</tr>
<tr>
<td>Confirmed lower extremity proximal DVT and/or PE for which parenteral LMWH is indicated for at least 6 months</td>
<td>Life expectancy &lt; 3 months</td>
</tr>
<tr>
<td>Thromboectomy, insertion of cava filter</td>
<td>Thromboectomy, insertion of cava filter</td>
</tr>
<tr>
<td>Treatment with another therapeutic anticoagulant other than that used for pretreatment prior to randomization</td>
<td>Treatment with another therapeutic anticoagulant other than that used for pretreatment prior to randomization</td>
</tr>
<tr>
<td>ECOG score of 3 or 4 at randomization</td>
<td>Primary Outcome</td>
</tr>
<tr>
<td>Composite of recurrent VTE and major bleeding during a 12 month study period</td>
<td>Was parenteral agent required before OAC #1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>AC #1</th>
<th>Edoxaban 60mg daily</th>
</tr>
</thead>
<tbody>
<tr>
<td>AC #2</td>
<td>Dalteparin</td>
</tr>
</tbody>
</table>

Ongoing DOAC Investigations

Prophylaxis
- High risk patient populations

Treatment
- Primary and delayed

Diversity in tumor types
- More heme populations being studied
Drug Interactions
VKA

Decrease INR
- Mercaptopurine
- Mitotane

Increased INR (see chart)

Warfarin and 5-FU
- Case reports support overall decrease during treatment (not just active weeks)

Root MM. Chemotherapy Newsletter Internal
Davis D. Pharmacotherapy 2005;25(3):442-447
DOACs

Rivaroxaban, edoxaban, and apixaban → CYP 3A4, PGP
  ◦ Tyrosine Kinase Inhibitors
    ◦ Imatinib, nilotinib, dasatinib

Functional considerations
  ◦ Bone marrow suppression (PLT depletion)
  ◦ Caution with thrombocytosis
VKA & DOACs

Nausea & Vomiting

**High (>90%)**
- Doxorubicin/cyclophosphamide
- Cyclophosphamide (>1500mg/m2)
- Doxorubicin (>60mg/m2)
- Carmustine (>250mg/m2)
- Epirubicin (>90mg/m2)
- Ifosfamide (>2 grams/m2)
- Mechlorethamine
- Streptozocin

**Moderate (30-90%)**
- Aldesleukin (>12-15 mil IU/m2)
- Amifostine (>300mg/m2)
- Arsenic Trioxide
- Azactidine
- Bendamustine
- Busulfan
- Carboplatin
- Carmustine
- Clofarabine
- Cyclophosphamide
- Cytarabine (>200mg/m2)
- Dactinomycin
- Daunorobucin
- Dinutuximab
- Doxorubicin
- Epirubicin
- Idarubicin
- Ifosfamide
- Irinotecan
- Melphalan
- Methotrexate (>250mg/m2)
- Oxaliplatin
- Temozolomide
- Trabectedin

Platinum agents can cause delayed N/V

Radiation considerations

NCCN Guidelines Version 1.2016 Antiemesis
VKA & DOACs

Mucositis – 40% solid tumors, 76% BMT, can’t forget radiotherapy
- Busulfan, thiotepa, procarbazine, cyclophosphamide
- Anthracyclines
- 5-FU, methotrexate, hydroxyurea
- Everolimus

Dysgeusia and taste aversion
- Taste aversion → changes in appetite
- Platinum agents

Diarrhea
- EGFR agents
- Irinotecan (atropine)
- Capecitabine and 5-FU

<table>
<thead>
<tr>
<th></th>
<th>Chemo</th>
<th>Chemo + RT</th>
<th>RT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mucositis</td>
<td>50%</td>
<td>75%</td>
<td>66%</td>
</tr>
</tbody>
</table>

Chemo = chemotherapy, RT = radiation therapy

Patient Factors
Patient Case

RW is a 67 year old white female who presents to the hospital with CC of uni-lateral lower extremity edema. She is diagnosed with a DVT. She is started on a heparin drip.

PMH: obese (BMI 35)

SH: non-smoker, non-drinker, married, works fulltime as a MSW

Home medications: none

PE: abdominal discomfort with complaints of prolonged constipation, she has never had a colonoscopy
Patient Case

RW is undergoes extensive work-up for colon cancer and is found to have: metastatic adenocarcinoma of the sigmoid colon, with mets in the liver and lung.

Discussion Question:

1) What risk factors does RW have for DVT? What cancer-specific risk factors does she have?

2) What ECOG status is RW?
Patient Case

RW will go home and follow-up for FOLFOX treatment as an outpatient. She requires home-going anticoagulation therapy, and her insurance will not cover LMWH. The physician asks you to transition her to warfarin.

Discussion Questions:

1. Is warfarin the best option for RW? If so, what is your dosing strategy?

2. If warfarin is not used, which agent would you choose?
## Patient Case

<table>
<thead>
<tr>
<th>Day</th>
<th>INR</th>
<th>Dosing</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 2</td>
<td>1.1</td>
<td>5 mg x 4 days</td>
<td>Day 2 of new start, 3 days after cycle #1, + decreased appetite, dizziness</td>
</tr>
<tr>
<td>Day 5</td>
<td>2.5</td>
<td>2.5 mg x 1 day, 5 mg x 2 days</td>
<td>Stopped Lovenox bridge (total 5 day duration), + decreased appetite, dizziness</td>
</tr>
<tr>
<td>Day 8</td>
<td>3.5</td>
<td>2.5 mg x 2 days, 5 mg x 2 days</td>
<td>+ worsening dizziness</td>
</tr>
<tr>
<td>Day 12</td>
<td>4.0</td>
<td>Hold x 1 day, 2.5 mg x 2 days</td>
<td>Scheduled cycle #2, held for low ANC, + chest pain, dizziness, decreased appetite</td>
</tr>
<tr>
<td>Day 15</td>
<td>2.4</td>
<td>5 mg, 2.5 mg x 2 days, 5 mg</td>
<td>+ dizziness, fatigue, chest pain</td>
</tr>
<tr>
<td>Day 21</td>
<td>3.2</td>
<td>5 mg daily except 2.5 mg MWF</td>
<td>2 days after cycle #2, + chest pain, dizziness</td>
</tr>
<tr>
<td>Day 28</td>
<td>3.1</td>
<td>5 mg daily except 2.5 mg MWF</td>
<td>+ decreased appetite, dizziness</td>
</tr>
<tr>
<td>Day 36</td>
<td>5.3</td>
<td>Hold x 1 day, 5 mg daily except 2.5 mg MWF</td>
<td>3 days after cycle #3, + light headed, chest pain, nausea</td>
</tr>
<tr>
<td>Day 40</td>
<td>2.8</td>
<td>2.5 mg daily except 5 mg Tues, Thurs, Sat</td>
<td>+ fatigue, decreased appetite, chest pain</td>
</tr>
</tbody>
</table>
## Cost Considerations (estimates)

<table>
<thead>
<tr>
<th>Medication</th>
<th>Cost per 30 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apixaban</td>
<td>$400</td>
</tr>
<tr>
<td>Dabigatran</td>
<td>$400</td>
</tr>
<tr>
<td>Edoxaban</td>
<td>$350</td>
</tr>
<tr>
<td>Enoxaparin</td>
<td>$1200</td>
</tr>
<tr>
<td>Fondaparinux</td>
<td>$4000</td>
</tr>
<tr>
<td>Rivaroxaban</td>
<td>$650 to start then $400</td>
</tr>
<tr>
<td>Warfarin</td>
<td>$25 (on some $4 lists)</td>
</tr>
</tbody>
</table>
Resources to Help with Costs for DOACs

• 30 day free trial card
  • Available for all DOACS
    • 1 per lifetime
  • Okay to use for ALL patients
    • Cash/uninsured, Medicare, Medicaid, Private Insurance

• Copay cards
  • Unable to use for Medicare or Medicaid patients
  • **Apixaban** → $10/month x 2 years, patient would be eligible for future cards
    • Able to ask for patient assistance when you call to activate card
  • **Dabigatran** → $0/month x 1 year
  • **Edoxaban** → $4/month x 1 year
  • **Rivaroxaban** → $0/month x 1 year
Considerations in CKD Patients

% Renal Clearance

- Apixaban – 27%
- Edoxaban – 40%
- Rivaroxaban – 66%
- Dabigatran – 80%

Savaysa. [package insert]. Tokyo, Japan. Daiichi Sankyo Co. LTD. 20
Patient Case

After 3 months of therapy, RW is diagnosed with a recurrent VTE. She presents with a PE.

Discussion Question:

1. What is the best option for RW now?
Assessment Question #1

What ECOG performance status range was excluded in the CLOT trial?

a. ECOG 2+
b. ECOG 3+
c. ECOG 4+
d. ECOG 5+
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What ECOG performance status range was excluded in the CLOT trial?

a. ECOG 2+

b. ECOG 3+

c. ECOG 4+

d. ECOG 5+
Assessment Question #2

Which patient population(s) have minimal data related to the safety and efficacy of DOACS in the treatment of VTE?

a. Brain cancer
b. Hematological cancers
c. Lung cancer
d. A and B
e. B and C
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b. Hematological cancers
c. Lung cancer
d. A and B
e. B and C
Direct Oral Anticoagulants as an Alternative to Warfarin Therapy in Oncology Patients

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