Direct Oral Anticoagulants: Are Ready for Prime Time in Cancer Patients with VTE

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Friday
1:24 PM-1:29 PM

Disclosure
Financial Relationships
Geno J. Merli, MD, MACP, FHM, FSVM

- Janssen: Research MARINER Study (complete)
- Bristol-Meyer Squibb: ADIOS Study (complete)
- Portola: APEX Study (complete)
- LoweRisk LLC, Co-Chief Development Officer

Einstein PE + DVT
Pooled Analysis: Active Cancer Patients

<table>
<thead>
<tr>
<th>Recurrent VTE</th>
<th>Rate</th>
<th>LMWH + Warf</th>
<th>HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer</td>
<td>24/316</td>
<td>20/281</td>
<td>0.80 (0.56-1.13)</td>
</tr>
<tr>
<td>Major Bleeding</td>
<td>9/316</td>
<td>16/278</td>
<td>0.53 (0.33-0.82)</td>
</tr>
</tbody>
</table>


AMPLIFY Study
Patients with Cancer

<table>
<thead>
<tr>
<th>Objective Confirmed</th>
<th>LMWH</th>
<th>Edoxaban 60 mg QD</th>
<th>Risk Difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recurrent VTE</td>
<td>34/522</td>
<td>54/524</td>
<td>-3.8 (-7.1, -0.4)</td>
</tr>
<tr>
<td>Confirmed Fatal</td>
<td>0/522</td>
<td>2/524</td>
<td>-1.4 (-9.8, 6.9)</td>
</tr>
<tr>
<td>DVT only</td>
<td>13/522</td>
<td>30/524</td>
<td>-1.7 (-7.0, 3.7)</td>
</tr>
<tr>
<td>Symptomatic</td>
<td>22/522</td>
<td>40/524</td>
<td>-1.8 (-6.0, 2.4)</td>
</tr>
<tr>
<td>Major Bleeding</td>
<td>33/522</td>
<td>17/524</td>
<td>3.1 (0.5, 5.7)</td>
</tr>
<tr>
<td>Confirmed Fatal</td>
<td>0/522</td>
<td>2/524</td>
<td>-1.2 (-10.2, 7.9)</td>
</tr>
</tbody>
</table>

Hokusai Cancer Study

<table>
<thead>
<tr>
<th>Thrombus (n=114)</th>
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Hokusai Cancer Study

| Thrombus (n=114) |

Rivaroxaban
15 mg BID for 3 weeks, then 20 mg QD, for 6 months total

Dalteparin
200 IU/kg QD for 1 month, then 150 IU/kg for months 2–6


The primary outcome was VTE recurrence over 6 months. Safety was assessed by major bleeding and clinically relevant non-major bleeding (CRNMB).

SELECT-D
Recurrent VTE

HR: 0.43 (95% CI: 0.19, 0.99)


SELECT-D
Major Bleeding

ADAM Study Design: Safety of Apixaban With Cancer-Related VTE

• Select exclusion criteria
  • Age >10 years
  • Confirmed acute lower or upper extremity VTE, PE, splanchnic or cerebral vein thrombosis
  • Treatment of a thromboembolic event ≤6 months prior to randomization
  • Active cancer

• Inclusion criteria
  • Age ≥18 years
  • Confirmed acute lower or upper extremity DVT, PE, splanchnic or cerebral vein thrombosis
  • Active cancer

• Treatment of a thromboembolic event ≤6 months prior to randomization
• Major bleeding events that occur during treatment or within 7 days of treatment discontinuation (on-treatment analysis)
• Key secondary outcome
  • Major or CRNMB bleeding events that occur during treatment or within 7 days of treatment discontinuation (on-treatment analysis)
  • Time to the first event of the composite VTE recurrence, including DVT, PE, fatal PE, or arterial thromboembolism

Cancer-Associated VTE (CAT)
Treatment Guidelines

Guideline/Recommendation

• ASCO, 2015
  • LMWH recommended for more than 5–10 days of established VTE and for long-term secondary prophylaxis
  • LMWH does not recommend for patients with malignancy and VTE

• ACCP, 2016
  • Leg DVT or PE and cancer: suggest LMWH over VKA (Grade 2B) or dabigatran, rivaroxaban, apixaban, or edoxaban (all 2C)
  • No high bleeding risk: recommend extended anticoagulation (2C)
  • High bleeding risk: suggest extended anticoagulation (tt extended stop date) and 5 months of treatment (2C)

• NCCN, 2018
  • Treatment options for CAT include
    – Monotherapy: LMWH (preferred, category 2A; dalteparin, 1); rivaroxaban (2A); fondaparinux (2A); UFH (2B); apixaban for patients who refuse or have compelling reasons to avoid LMWH (2A)
    – Combination therapy: LMWH + edoxaban (category 1); LMWH + warfarin, fondaparinux + warfarin, UFH + warfarin, UFH + edoxaban, LMWH + dabigatran, UFH + dabigatran (all category 2A)
  • Minimum duration of therapy is 3 months

• ISTH, 2018
  • Patients with cancer, acute VTE diagnosis, low bleeding risk, and no drug-drug interactions with concomitant medications
  • Treatment of a thromboembolic event ≤6 months: LMWH + edoxaban (2A)
  • No high bleeding risk: recommend extended anticoagulation (2C)

Yes, DOACs are ready for Prime Time
• Selection based on cancer important
• Accepting the risk of major bleeding
• Must consider concomitant chemo and ability to tolerate oral therapy

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Direct Oral Anticoagulants & Cancer
READY For Prime Time

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