Venous Thromboembolism Management in Ambulatory Patients with Cancer: Dawn of the Oral Anticoagulant Era?

Sarah L. Hanson, PharmD; Christina Maher, PharmD; Jai N. Patel, PharmD, BCOP

**BACKGROUND:** Venous thromboembolism (VTE), consisting of deep-vein thrombosis or pulmonary embolism, is a common yet underrecognized complication of cancer. VTE in patients with cancer accounts for approximately 20% of all VTE events in the United States. The diagnosis of cancer increases VTE risk by more than 4-fold, and VTE is the second leading cause of death in patients with cancer.

**OBJECTIVE:** To review the management of VTE in patients with cancer, including prophylaxis and treatment, based on recently published randomized clinical trials, with a focus on DOACs.

**DISCUSSION:** The PROTECHT and SAVE-ONCO clinical trials demonstrated statistically significant reductions in the incidence of VTE with low-molecular-weight heparin (LMWH) as primary prevention in ambulatory patients with cancer; however, the magnitude of VTE reduction did not prompt a change in clinical practice guidelines. The AVERT and CASSINI clinical trials enrolled patients with a Khorana risk score ≥2 and demonstrated that DOACs are safe and effective options to reduce VTE risk. The SELECT-D, Hokusai VTE Cancer, and ADAM VTE clinical trials compared the use of DOACs and LMWH in the prevention of VTE recurrence in patients with cancer. The results demonstrated that DOACs were more effective than LMWH but with an increased risk for bleeding in some patients.

**CONCLUSION:** A concerted effort should be made by all healthcare professionals caring for ambulatory patients with cancer to screen patients for VTE risk factors and to consider interventions if clinically appropriate.

**KEY WORDS:** direct oral anticoagulant, Khorana risk score, low-molecular-weight heparin, patients with cancer, thromboprophylaxis, venous thromboembolism
Table 1  Risk Factors for VTE in Patients with Cancer

<table>
<thead>
<tr>
<th>Tumor type</th>
<th>Oncology therapy-related risks</th>
<th>Treatment-related risks</th>
<th>Patient-specific risks</th>
<th>Biomarkers-related risks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very high risk:</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Pancreatic</td>
<td>Platinum-based chemotherapy L-asparaginase&lt;sup&gt;a&lt;/sup&gt;</td>
<td>ESA agents</td>
<td>Older age</td>
<td>Platelets &gt;350,000/μL</td>
</tr>
<tr>
<td>Gastrointestinal Brain</td>
<td>Mitomycin C&lt;sup&gt;b&lt;/sup&gt; Immunomodulatory agents (ie, lenalidomide, thalidomide, pomalidomide)</td>
<td>Transfusions Indwelling venous access devices Radiation therapy Use of G-CSF&lt;sup&gt;c&lt;/sup&gt; Surgery&lt;sup&gt;d&lt;/sup&gt;</td>
<td>Race</td>
<td>Leukocytes &gt;11,000/μL</td>
</tr>
<tr>
<td>High risk:</td>
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<tr>
<td>Lung</td>
<td></td>
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<tr>
<td>Gynecologic Bladder</td>
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<td></td>
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<tr>
<td>Testicular</td>
<td>SERMs&lt;sup&gt;e&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Renal</td>
<td></td>
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<tr>
<td>Lymphoma</td>
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<tr>
<td>Other biomarkers (D-dimer, P-selectin, tissue factor)</td>
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</tr>
</tbody>
</table>

BMI indicates body mass index; ESA, erythropoiesis-stimulating agent; G-CSF, granulocyte colony-stimulating factor; SERM, selective estrogen receptor modulator; VTE, venous thromboembolism.

Clinical Trials on VTE Prophylaxis

Few studies have investigated the impact of VTE prophylaxis in ambulatory patients with cancer (Table 2).<sup>16-20</sup> The PROTECHT and SAVE-ONCO clinical trials demonstrated statistically significant reductions in VTE incidence with LMWH as primary prevention in ambulatory patients with cancer (Table 2).<sup>16,17</sup> In the PROTECHT study, most subgroups showed lower rates of VTE with the use of nadroparin compared with placebo, except for the pancreatic cancer group.<sup>16</sup> The SAVE-ONCO study stratified VTE by cancer type, stage, and baseline risk.<sup>17</sup> In neither trial did the investigators use a risk assessment tool for enrollment.

Although the primary end points in PROTECHT and SAVE-ONCO met their statistical threshold,<sup>16,17</sup> the results did not radically change prescribing practices or prompt clinical practice guideline updates, given the low magnitude of VTE reduction. Based on a low benefit-risk profile, the guidelines for VTE prophylaxis did not change.

Two recent trials evaluated use of DOACs to prevent VTE in high-risk, ambulatory patients with cancer. The AVERT clinical trial investigated the use of apixaban for VTE prevention, whereas the CASSINI clinical trial investigated rivaroxaban in a similar setting (Table 2).<sup>17,18</sup> Both studies required KPS of ≥2 to target patients at high risk for VTE. Although both studies showed efficacy in preventing VTE, the differences in study design, population, and screening were notable.<sup>18,19</sup>

The CASSINI study enrolled a large number of patients with pancreatic and gastric cancers, both known to pose a very high VTE risk compared with the AVERT study, which had an increased rate of gynecologic cancers and lymphoma.<sup>18,19</sup> CASSINI excluded 4.5% (N = 49) of patients presenting with baseline asymptomatic VTE, having relatively stringent inclusion criteria, but that did not reflect a real-world population, because baseline ultrasound screening is not done routinely in clinical practice.<sup>19</sup> Patients in the AVERT study did not undergo baseline ultrasound screening.<sup>18</sup>

Screening differences between the 2 studies highlight the potential for variance in primary outcomes, potentially resulting in lower overall event rates in the CASSINI study.<sup>19</sup> Patients in the AVERT study might have received benefit from apixaban for the treatment...
Table 2: Summary of VTE Prophylaxis Clinical Trials in Ambulatory Patients with Cancer

<table>
<thead>
<tr>
<th>Clinical trial</th>
<th>Study population</th>
<th>Treatment</th>
<th>Primary end point</th>
<th>Primary outcome (efficacy)</th>
<th>Number needed to treat, N</th>
<th>Safety (bleeding)</th>
<th>Number needed to harm, N</th>
</tr>
</thead>
<tbody>
<tr>
<td>PROTECHT (Agnelli et al, 2009)</td>
<td>Tumor type: lung (24.3%), gastrointestinal (20.4%) No risk stratification tool used for inclusion</td>
<td>Nadroprin 3800 IU anti-Xa once daily or placebo</td>
<td>Composite of symptomatic venous or arterial thromboembolic events</td>
<td>15:769 (2.0%) nadroprin vs 15:381 (3.9%) placebo (one-sided 95% CI, 0.303)</td>
<td>Single-sided P = .02</td>
<td>53</td>
<td>Major bleeding: 5:769 (0.7%) nadroprin vs 0 (0%) placebo</td>
</tr>
<tr>
<td>SAVE-ONCO (Agnelli et al, 2012)</td>
<td>Tumor type: lung (36.6%), colon (28.9%) No risk stratification tool used for inclusion</td>
<td>Semuloparin 20 mg once daily or placebo</td>
<td>Composite of any symptomatic DVT, any nonfatal pulmonary embolism, and death related to VTE</td>
<td>20:1608 (1.2%) semuloparin vs 55:1604 (3.4%) placebo (HR, 0.36; 95% CI, 0.21-0.60)</td>
<td>P &lt;.001</td>
<td>46</td>
<td>Major bleeding: 19:1589 (1.2%) semuloparin vs 18:1583 (1.1%) placebo (HR, 1.05; 95% CI, 0.55-1.99)</td>
</tr>
<tr>
<td>AVERT (Carrier et al, 2019)</td>
<td>Tumor types: lymphoma (26.1%), gynecologic (25.4%) KRS ≥2</td>
<td>Apixaban 2.5 mg twice daily or placebo</td>
<td>Objectively documented VTE over 180-day follow-up period</td>
<td>12:288 (4.2%) apixaban vs 28:275 (10.2%) placebo (HR, 0.41; 95% CI, 0.26-0.65)</td>
<td>P &lt;.001</td>
<td>53</td>
<td>During treatment period: 3:288 (1.0%) apixaban vs 20:275 (7.3%) placebo (HR, 0.14; 95% CI, 0.05-0.42)</td>
</tr>
<tr>
<td>CASSINI (Khorana et al, 2019)</td>
<td>Tumor types: pancreatic (32.8%), gastric (20.7%), lung (17.1%) KRS ≥2</td>
<td>Rivaroxaban 10 mg daily or placebo</td>
<td>Composite of objectively confirmed symptomatic or asymptomatic lower-extremity proximal DVT, symptomatic upper- or lower-extremity distal DVT, symptomatic or incidental pulmonary embolism and VTE-related death</td>
<td>Primary: 25:420 (6.0%) rivaroxaban vs 37:421 (8.8%) placebo (HR, 0.66; 95% CI, 0.40-1.09)</td>
<td>P = .10</td>
<td>36</td>
<td>During treatment period: 11:420 (2.6%) rivaroxaban vs 27:421 (6.4%) placebo (HR, 0.40; 95% CI, 0.20-0.80)</td>
</tr>
<tr>
<td>Gemcitabine ± dalteparin (Marayevas et al, 2012)</td>
<td>Pancreatic cancer: nonresectable, recurrent, or metastatic pancreatic adenocarcinoma No incidental imaging evidence of VTE at entry</td>
<td>Dalteparin + gemcitabine or gemcitabine alone</td>
<td>Incidence of all-type VTE during the study period of 12 weeks (84 days), and through the entire follow-up period (&lt;100 days from randomization)</td>
<td>14:62 (23%) gemcitabine vs 2:59 (3.4%) gemcitabine + dalteparin (HR, 0.145; 95% CI, 0.035-0.612)</td>
<td>P = .002</td>
<td>5</td>
<td>ISTH severe bleeding: 2/62 (3%) gemcitabine vs 2/59 (3%) gemcitabine + dalteparin</td>
</tr>
</tbody>
</table>

*Only main tumor types included in the table, not exhaustive.
CI indicates confidence interval; DVT, deep-vein thrombosis; HR, hazard ratio; ISTH, International Society on Thrombosis and Haemostasis; KRS, Khorana risk score; N/A, not available; VTE, venous thromboembolism.
Table 3  Summary of VTE Treatment in Clinical Trials of Oncology Patients

<table>
<thead>
<tr>
<th>Clinical trial</th>
<th>Study population</th>
<th>Treatment</th>
<th>Primary end point</th>
<th>Efficacy (primary outcome)</th>
<th>Number needed to treat, N</th>
<th>Safety (bleeding)</th>
<th>Number needed to harm, N</th>
</tr>
</thead>
<tbody>
<tr>
<td>SELECT-D (Young et al, 2018)</td>
<td>Tumor types: colorectal (25.1%), lung (11.5%), breast (9.9%)</td>
<td>Dalteparin 200 IU/kg daily in month 1, then 150 IU/kg daily for months 2-6 or rivaroxaban 15 mg twice daily for 3 weeks, then 20 mg daily for 6 months</td>
<td>VTE recurrence over 6 months (4%) in rivaroxaban vs (11%) in dalteparin (HR, 0.43; 95% CI, 0.19-0.99)</td>
<td>14</td>
<td>Major bleeding: 11:203 (6%) rivaroxaban vs 6:203 (4%) dalteparin (HR, 1.83; 95% CI, 0.68-4.96)</td>
<td>50</td>
<td>35</td>
</tr>
<tr>
<td>Hokusai (Raskob et al, 2018)</td>
<td>Metastatic disease, 554:1046 (53%); recurrent cancer, 315:1046 (30.1%)</td>
<td>Dalteparin 60 mg daily or dalteparin 200 IU/kg SC daily for 30 days</td>
<td>Composite of recurrent VTE or major bleeding in 12 months after randomization</td>
<td>143</td>
<td>Major bleeding: 36:522 (6.9%) vs 21:524 (4.0%) (HR, 1.77; 95% CI, 1.03-3.04)</td>
<td>35</td>
<td>71 (based on primary outcome of major bleeding)</td>
</tr>
<tr>
<td>ADAM VTE (McBane et al, 2019)</td>
<td>Tumor types: colorectal (12.2%), breast (10.9%), pancreatic/hepatobiliary (15.0%), gynecologic (9.5%)</td>
<td>Apixaban 10 mg twice daily for 7 days, then 5 mg twice daily for 6 months or dalteparin 200 IU/kg for 1 month, then 150 IU/kg once daily</td>
<td>Primary: major bleeding, including fatal Secondary: recurrent VTE, composite of major bleeding + clinically relevant nonmajor bleeding</td>
<td>18 (based on secondary outcome of recurrent VTE)</td>
<td>Secondary major bleeding + clinically relevant nonmajor bleeding: 9:145 (6.2%) apixaban vs 9:142 (6.3%) dalteparin (HR, 0.931; 95% CI, 0.43-2.02)</td>
<td>71 (based on primary outcome of major bleeding)</td>
<td>0.0281</td>
</tr>
</tbody>
</table>

*Only main tumor types included in the table, not exhaustive.

1 NTN is based on DOAC = experimental arm and LMWH = control arm, and refers to the primary outcome except for ADAM VTE as noted.

2 CI indicates confidence interval; DOAC, direct oral anticoagulant; HR, hazard ratio; LMWH, low-molecular-weight heparin; NNT, number needed to treat; SC, subcutaneous; VTE, venous thromboembolism.

of an asymptomatic VTE that was present at baseline.18

AVERT demonstrated a statistically significant difference in the primary outcome of VTE reduction in the modified intention-to-treat population, or in all randomized patients who received at least 1 dose of the study drug.18 CASSINI did not show a significant difference in the primary outcome of VTE reduction in the intention-to-treat population, which included all randomized patients, regardless of drug administration.19 Notably, a statistically significant reduction in VTE was found in the prespecified treated population in CASSINI.19 Both studies had high discontinuation rates—37% in the AVERT study and 47% in the CAS-

SINI study. Nearly 40% of events in CASSINI were in patients after treatment discontinuation. Adverse events did not contribute to discontinuation and were not different between the placebo versus the active treatment groups.18,19

One prospective pilot study evaluated the use of apixaban 2.5 mg twice daily for 6 months in patients with multiple myeloma who received first-line thalido-
mide-based treatment or second-line lenalidomide-based treatment.19 Among the 104 patients, 2 venous thrombotic events were registered. In all, 1 major and 11 clinically relevant nonmajor bleeding events were reported, demonstrating that apixaban may be effective and safe in preventing VTE in patients with multiple myeloma who receive treatment with immunomodulatory drugs.21

Currently, 2 randomized clinical trials, one with rivaroxaban versus aspirin (NCT03428373) and one with apixaban versus placebo (NCT02958969), are underway.22,23

Venous Thromboembolism Treatment Trials

Although DOACs are not recommended for use as routine primary VTE prophylaxis in all patients with cancer, they are emerging for use for VTE treatment or to reduce VTE recurrence.2 Table 3 summarizes major clinical trials with DOACs used for VTE treatment.24,26
### Table 4 Summary of Current Recommendations for Direct Oral Anticoagulants

<table>
<thead>
<tr>
<th>Generics/brand names</th>
<th>Dabigatran (Pradaxa)</th>
<th>Rivaroxaban (Xarelto)</th>
<th>Apixaban (Eliquis)</th>
<th>Edoxaban (Savaysa)</th>
<th>Betrixaban (Bevyxxa)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Available dosages</td>
<td>150 mg, 75 mg</td>
<td>10 mg</td>
<td>5 mg</td>
<td>30 mg, 15 mg</td>
<td>40 mg, 80 mg</td>
</tr>
<tr>
<td>AF dosing (normal renal function)</td>
<td>CrCl 15 mL/min-30 mL/Hr</td>
<td>CrCl 15 mL/min-50 mL/Hr</td>
<td>CrCl &lt;15 mL/min: avoid use</td>
<td>CrCl 15 mL/min-50 mL/Hr</td>
<td></td>
</tr>
<tr>
<td>AF dosing (impaired renal function)</td>
<td>CrCl &lt;30 mL/min: avoid use</td>
<td>CrCl &gt;30 mL/min: CrCl &gt;30 mL/min: avoid use</td>
<td>CrCl &lt;15 mL/min: avoid use</td>
<td>CrCl &gt;30 mL/min: avoid use</td>
<td></td>
</tr>
<tr>
<td>DVT/PE treatment</td>
<td>150 mg twice daily after 5-10 days of parenteral therapy</td>
<td>Postoperative prophylaxis in hip replacement</td>
<td>15 mg twice daily</td>
<td>10 mg twice daily</td>
<td>150 mg twice daily</td>
</tr>
<tr>
<td>DVT prophylaxis</td>
<td>Postoperative prophylaxis in hip replacement</td>
<td>Postoperative prophylaxis in hip replacement</td>
<td>15 mg twice daily</td>
<td>15 mg twice daily</td>
<td>150 mg twice daily</td>
</tr>
<tr>
<td>Dosing adjustment in liver dysfunction based on Child-Pugh</td>
<td>A No dose adjustment</td>
<td>No dose adjustment</td>
<td>No dose adjustment</td>
<td>No dose adjustment</td>
<td>No dose adjustment</td>
</tr>
<tr>
<td>Contraindications</td>
<td>Active pathologic bleeding or hypersensitivity to medication or components</td>
<td>Mechanical prosthetic heart valves</td>
<td>Drug interactions</td>
<td>Avoid use w/ rifampin</td>
<td>Decrease dose to 30 mg daily w/ verapamil, quinidine, drotrecan, azithromycin, erythromycin, clarithromycin, telithromycin, or ketoconazole</td>
</tr>
<tr>
<td>Clinical pearls</td>
<td>Direct thrombin inhibitor, has potential to prolong aPTT</td>
<td>Recently indicated for CAD/PAD, 2.5 mg twice daily + low-dose aspirin</td>
<td>Decrease dose by 50% from 5 or 10 mg and avoid coadministration of 2.5 mg twice daily w/ telithromycin, or ritonavir, or clarithromycin</td>
<td>Avoid if CrCl &gt;95 mL/min</td>
<td>Use w/ food same time each day</td>
</tr>
<tr>
<td>Reversal agent</td>
<td>Idarucizumab (Praxbind)</td>
<td>Andexanet alfa (Andexa)</td>
<td>Not studied</td>
<td>Not studied</td>
<td>Not studied</td>
</tr>
</tbody>
</table>

*Can reduce to 10 mg daily after at least 6 months of standard anticoagulation therapy.

AF indicates atrial fibrillation; aPTT, activated partial thromboplastin time; CAD, coronary artery disease; CrCl, creatinine clearance; DVT, deep-vein thrombosis; ESRD, end-stage renal disease; GI, gastrointestinal; LFT, liver function test; PAD, peripheral artery disease; PE, pulmonary embolism; P-gp, P-glycoprotein; SCR, serum creatinine; THA, total hip arthroplasty; TKA, total knee arthroplasty; VTE, venous thromboembolism.

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The SELECT-D clinical trial demonstrated a decreased rate of recurrent VTE with rivaroxaban compared with dalteparin (4% vs 11%, respectively; hazard ratio [HR], 0.43; 95% confidence interval [CI], 0.19-0.99), but an increase in clinically relevant nonmajor bleeding events (HR, 3.76; 95% CI, 1.63-8.69). Based on the results from this study, the updated 2020 NCCN clinical guidelines include rivaroxaban as an option for VTE treatment for patients with cancer.12,24

Similarly, the Hokusai VTE Cancer clinical trial determined that edoxaban was noninferior to dalteparin with respect to a composite end point of recurrent VTE or major bleeding (edoxaban, 12.8% vs dalteparin, 13.5%; HR, 0.97; 95% CI, 0.70-1.36).25 Edoxaban had lower VTE recurrence rates but higher rates of bleeding.25 Edoxaban is now also included as an option for the treatment of VTE in the NCCN guidelines after the completion of at least 5 days of LMWH or unfractionated heparin therapy.12

The investigator-initiated ADAM VTE clinical trial identified lower rates of recurrent VTE with apixaban versus dalteparin (0.7% vs 6.3%, respectively; HR, 0.099; 95% CI, 0.013-0.780; \(P = .0281\)), and lower bleeding rates were noted in the apixaban group (apixaban 0% vs dalteparin 1.4%; \(P = .138\)).26 Based on these study results, apixaban is included in the NCCN guidelines as a second-line option for VTE treatment for patients who refuse or are intolerant of treatment with LMWH.15,26

**Clinical Considerations**

In light of these recent clinical trials supporting the use of DOAC for VTE prophylaxis and treatment, the updated ASCO 2019 guidelines include the use of rivaroxaban and apixaban as thromboprophylaxis options for patients at high risk for VTE, as well as the addition of rivaroxaban and edoxaban as VTE treatment options.10 Specifically, the use of DOAC is mentioned as a prophylaxis option for those at high risk, which is defined by a pretreatment KRS of 2.10

Utilizing KRS screening or incorporating a system with frequent monitoring for VTE symptoms may be warranted, given the high risk for VTE in the ambulatory oncology setting. For example, one study showed a high rate (8.5%) of baseline asymptomatic VTE in patients with a KRS of 3, suggesting that upfront ultrasonography may be beneficial in very high-risk patients.27

ASCO was the first organization to incorporate DOACs into its guideline recommendations and to consider those agents for upfront thromboprophylaxis in high-risk outpatients.10 The NCCN guidelines were also updated to include apixaban and rivaroxaban as VTE prophylaxis options in intermediate- or high-risk patients based on KRS of 2, and added apixaban, edoxaban, and rivaroxaban as VTE treatment options for oncology patients.12 We expect that other organizations may follow suit.

Although DOACs offer a more convenient administration method than the daily injections required with LMWH, the decision to use DOACs should involve the evaluation of patient-specific factors, such as renal and hepatic function, drug interactions, insurance coverage, and bleeding risk (particularly in those with gastrointestinal cancers).

**Table 4** provides summaries of important information about DOACs regarding dosing, contraindications, drug interactions, and other clinical pearls that are highly relevant to pharmacy practice.12,28-32 Of the DOACs studied for VTE prophylaxis in ambulatory patients with cancer, only rivaroxaban should be avoided in the setting of renal impairment, when the creatinine clearance decreases to \(\leq\)15 mL/min.28-32 The prescribing information for apixaban and for rivaroxaban suggest that strong inhibitors or inducers of P-glycoprotein or cytochrome P3A4 can increase or decrease drug concentrations and potentially alter the safety and efficacy of these drugs.29,30

Whereas KRS was used in the AVERT and the CASSINI studies, no standard guideline recommendation exists for KRS screening frequency, timing, or appropriateness for specific tumor types.18,19 Although some experts believe that KRS may be improved as a risk stratification tool by incorporating performance status, biomarker measurements, and chemotherapy type,21 KRS continues to be widely recognized as a user-friendly and simple screening modality.34

The major limitations of KRS include the requirement for multiple laboratory parameters and inclusion of specific tumor types.7 KRS does not include hematologic malignancies and does not utilize other validated markers, such as D-dimer or clinical factors such as history of VTE. Other tools are scores used in the CONKO, PROTECHT, and the Vienna Cancer and Thrombosis Study (CATS).6,35-37

In a comparative analysis, the PROTECHT16,36 and the Vienna CATS scores35 demonstrated better efficacy in discerning between high- and low-risk patients than the KRS tool.6 D-dimer results from the Vienna CATS35 and the use of gemcitabine or platinum-based chemotherapy from the PROTECHT study16,36 were significantly associated with VTE risk.6

Creating a standardized tool that is applicable across all disease states and treatments may be beneficial to identify high-risk patients who could benefit from VTE prophylaxis. The ideal tool would strike the right bal-
ance between predictive utility and complexity or ease of use in practice. Embedding KRS or another risk stratification tool in the electronic medical record may help to trigger high-risk patients who would benefit from referral to a nonmalignant hematology specialist for consideration of screening ultrasonography or thromboprophylaxis.

Considering that KRS may not perform optimally in all tumor types, particularly in hematologic malignancies and even in some solid tumors, such as lung, a call for tumor-specific studies is warranted. A prospective trial comparing the use of gemcitabine with or without dalteparin in patients with pancreatic cancer demonstrated no fatal VTE in the dalteparin group compared with 5 (8.3%) of 62 patients in the gemcitabine-only group (P = .057), which suggests that upfront initiation of VTE prophylaxis in pancreatic cancer may impact VTE-related mortality rates. This study also noted reduced VTE with dalteparin, from 23% to 3.4%. Fewer studies exist across other solid tumors or hematologic malignancies.

VTE treatment studies comparing LMWH with DOACs demonstrated that DOACs are at least noninferior to LMWH, if not more effective, but may be associated with increased bleeding risk. Based on these data, DOACs are likely to be noninferior to LMWH for VTE prophylaxis, although it is unlikely that large randomized clinical trials will be conducted to confirm this.

As noted earlier, randomized clinical trials are ongoing to understand better the risk–benefit profile of administering DOACs in patients with multiple myeloma. This is especially the case when considering that aspirin prophylaxis alone is not sufficient to reduce VTE risk in most patients with multiple myeloma, along with the trend toward greater patient preference for DOACs versus LMWH.

Conclusion

Further research should optimize and standardize VTE risk stratification tools for clinical implementation, striking the right balance between drug efficacy and safety. The decision for thromboprophylaxis may also differ based on the timing of the cancer diagnosis, the treatment, and the tumor type. Nonetheless, a concerted effort should be made by all health professionals caring for patients with cancer to screen for VTE risk using available tools, such as KRS, as well as to consider appropriate interventions, including patient counseling on signs and symptoms of VTE, referral to a nonmalignant hematology specialist, screening ultrasound for baseline VTE, or thromboprophylaxis.

Author Disclosure Statement

Dr Hanson and Dr Maher have no conflicts of interest to report. Dr Patel is a Consultant to and has received research support/honoraria from Janssen Research & Development.

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