Introduction

• Among patients with malignancy, VTE is one of the leading causes of mortality

• Cancer increases VTE risk several-fold; inpatients and those receiving active therapy at greatest risk

• Incidence of VTE in cancer patients range from 4-20%

• Clinical rates may underrepresent burden; at autopsy, VTE rates in cancer patients as high as 50%

• Frequency of VTE appears to be increasing among cancer patients
ASCO Guideline Development Methodology

The ASCO Clinical Practice Guidelines Committee guideline process includes:

- a systematic literature review by ASCO guidelines staff
- an expert panel provides critical review and evidence interpretation to inform guideline recommendations
- final guideline approval by ASCO CPGC

The full ASCO Guideline methodology supplement can be found at: www.asco.org/guidelines/VTE
Risk Factors for cancer-related VTE

• Cancer-related
  – Primary site of malignancy
  – Stage *(risk increased with higher stage)*
  – Histology
  – Time since diagnosis *(risk increased during first 3-6 months)*

• Treatment-related
  – Chemotherapy, antiangiogenesis agents, hormonal therapy
  – Radiation therapy
  – Surgery ≥ 60 minutes
  – ESAs, transfusions
  – Indwelling venous access

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Risk Factors for cancer-related VTE

- **Patient-related**
  - Increased age
  - Ethnicity (*risk increased in African Americans*)
  - Co-morbidities (infection, renal and pulmonary disease, arterial thromboembolism, VTE history, inherited prothrombotic mutations)
  - Obesity
  - Performance status

- **Biomarkers**
  - Platelet count $\geq 350,000$/mm$^3$
  - Leukocyte count $> 11,000$/mm$^3$
  - Hemoglobin $< 10$ g/dL
Clinical Questions

(1) Should hospitalized patients with cancer receive anticoagulation for VTE prophylaxis?

(2) Should ambulatory patients with cancer receive anticoagulation for VTE prophylaxis during systemic chemotherapy?

(3) Should patients with cancer undergoing surgery receive perioperative VTE prophylaxis?

(4) What is the best method for treatment of patients with cancer with established VTE to prevent recurrence?

(5) Should patients with cancer receive anticoagulants in the absence of established VTE to improve survival?

(6) What is known about risk factors and risk prediction of VTE among patients with cancer?
Target Population

Medical and surgical oncologists, hospitalists, oncology nurses
Recommendations

Q1. Inpatient Prophylaxis

1.1 Hospitalized patients who have active malignancy with acute medical illness or reduced mobility should receive pharmacologic thromboprophylaxis in the absence of bleeding or other contraindications.

1.2 Hospitalized patients who have active malignancy without additional risk factors may be considered for pharmacologic thromboprophylaxis in the absence of bleeding or other contraindications.

1.3 Data are inadequate to support routine thromboprophylaxis in patients admitted for minor procedures or short chemotherapy infusion, or in patients undergoing stem cell/bone marrow transplantation.
2.1 Routine pharmacologic thromboprophylaxis is not recommended in cancer outpatients.

2.2 Based on limited RCT data, clinicians may consider LMWH prophylaxis on a case-by-case basis in highly selected outpatients with solid tumors receiving chemotherapy. Consideration of such therapy should be accompanied by a discussion with the patient about the uncertainty concerning benefits and harms, as well as dose and duration of prophylaxis in this setting.

2.3 Patients with multiple myeloma receiving thalidomide- or lenalidomide-based regimens with chemotherapy and/or dexamethasone should receive pharmacologic thromboprophylaxis with either aspirin or LMWH for lower-risk patients and LMWH for higher-risk patients.
Recommendations

Q3. Perioperative Prophylaxis

3.1 All patients with malignant disease undergoing major surgical intervention should be considered for pharmacologic thromboprophylaxis with either UFH or LMWH unless contraindicated because of active bleeding or a high bleeding risk.

3.2 Prophylaxis should be commenced preoperatively.

3.3 Mechanical methods may be added to pharmacologic thromboprophylaxis, but should not be used as monotherapy for VTE prevention unless pharmacologic methods are contraindicated because of active bleeding or high bleeding risk.

3.4 A combined regimen of pharmacologic and mechanical prophylaxis may improve efficacy, especially in the highest-risk patients.
3.5 Pharmacologic thromboprophylaxis for patients undergoing major surgery for cancer should be continued for at least 7-10 days. Extended prophylaxis with LMWH for up to 4 weeks postoperatively should be considered for patients undergoing major abdominal or pelvic surgery for cancer who have high-risk features such as restricted mobility, obesity, history of VTE, or with additional risk factors as listed in Table 3. In lower risk surgical settings, the decision on appropriate duration of thromboprophylaxis should be made on a case-by-case basis considering the individual patient.
Recommendations
Q4. Treatment and Secondary Prophylaxis

4.1 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).

4.2 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.

4.3 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.

4.4 The insertion of a vena cava filter is only indicated for patients with contraindications to anticoagulant therapy (see Table 4). It may be considered as an adjunct to anticoagulation in patients with progression of thrombosis (recurrent VTE or extension of existing thrombus) despite optimal therapy with LMWH.
4.5 For patients with primary CNS malignancies, anticoagulation is recommended for established VTE as described for other patients with cancer. Careful monitoring is necessary to limit the risk of hemorrhagic complications.

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

4.7 Based on consensus, incidental PE and DVT should be treated in the same manner as symptomatic VTE. Treatment of splanchnic or visceral vein thrombi diagnosed incidentally should be considered on a case-by-case basis, considering potential benefits and risks of anticoagulation.
5.1 Anticoagulants are not recommended to improve survival in patients with cancer without VTE

5.2 Patients with cancer should be encouraged to participate in clinical trials designed to evaluate anticoagulant therapy as an adjunct to standard anticancer therapies.
Recommendations

Q6. VTE Risk Assessment

6.1 Based on consensus, the Panel recommends that cancer patients should be assessed for VTE risk at the time of chemotherapy initiation and periodically thereafter. Individual risk factors, including biomarkers or cancer site, do not reliably identify cancer patients at high risk of VTE. In the outpatient setting, risk assessment can be conducted based on a validated risk assessment tool.

6.2 Based on consensus, the Panel recommends that oncologists educate patients regarding VTE, particularly in settings that increase risk such as major surgery, hospitalization, and while receiving systemic anti-neoplastic therapy.

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Absolute Contraindications to Therapeutic Anticoagulation in Cancer Patients with VTE

• Active major, serious or potentially life-threatening bleeding not reversible with medical or surgical intervention, including active bleeding in a critical site

• Severe, uncontrolled malignant hypertension

• Severe, uncompensated coagulopathy Severe platelet dysfunction or inherited bleeding disorder

• Persistent, severe thrombocytopenia (< 20,000/µL)

• Surgery or invasive procedure including lumbar puncture, spinal anesthesia, epidural catheter placement
Relative Contraindications to Therapeutic Anticoagulation in Cancer Patients with VTE

- Intracranial or spinal lesion at high risk of bleeding
- Active peptic or other GI ulceration at high risk of bleeding
- Active but non-life threatening bleeding
- Intracranial or CNS bleeding within 4 weeks
- Major surgery or serious bleeding within 2 weeks
- Persistent thrombocytopenia (< 50,000/µL)
Discussion

Patient - Clinician Communication

• Patients with cancer are often unaware of VTE signs and symptoms, and increased risk secondary to malignancy

• Patient education increases the likelihood of early intervention

• Patient education by the oncology team should include VTE warning signs and symptoms

• Education can help patients distinguish between underlying disease and potential VTE symptoms

• Ongoing communication, including H&P, can facilitate awareness of VTE

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Discussion
Future Directions

• Additional research is needed to clarify which cancer patients sufficiently benefit from prophylactic anticoagulation
  – Outpatients receiving chemotherapy
  – Patients undergoing bone marrow or stem cell transplant
  – Patients receiving hospice care

• Data to clarify the role of anticoagulants as an adjunct to anti-cancer therapy is also needed
Additional Resources

More information, including a Data Supplement, a Methodology Supplement, slide sets, and clinical tools and resources, is available at: www.asco.org/guidelines/VTE

Patient information is available at www.cancer.net
# ASCO Guideline Panel Members

<table>
<thead>
<tr>
<th>Member</th>
<th>Affiliation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anna Falanga, Co-Chair</td>
<td>Hospital Papa Giovanni XXIII</td>
</tr>
<tr>
<td>Gary H. Lyman, Co-Chair</td>
<td>Duke Cancer Institute</td>
</tr>
<tr>
<td>Alok A. Khorana</td>
<td>University of Rochester</td>
</tr>
<tr>
<td>Nicole M. Kuderer</td>
<td>Duke Cancer Institute</td>
</tr>
<tr>
<td>Juan Ignacio Arceus</td>
<td>University of Granada</td>
</tr>
<tr>
<td>Edward P. Balaban</td>
<td>University of Pittsburgh Cancer Centers</td>
</tr>
<tr>
<td>Jeffrey M. Clarke</td>
<td>Duke University</td>
</tr>
<tr>
<td>Christopher R. Flowers</td>
<td>Emory University School of Medicine</td>
</tr>
<tr>
<td>Charles W. Francis</td>
<td>University of Rochester</td>
</tr>
<tr>
<td>Leigh E. Gates</td>
<td>Patient Representative</td>
</tr>
<tr>
<td>Ajay K. Kakkar</td>
<td>Thrombosis Research Institute</td>
</tr>
<tr>
<td>Nigel Key</td>
<td>University of North Carolina</td>
</tr>
<tr>
<td>Agnes Y. Lee</td>
<td>University of British Columbia</td>
</tr>
<tr>
<td>Mark N. Levine</td>
<td>McMaster University</td>
</tr>
<tr>
<td>Howard A. Liebman</td>
<td>University of Southern California</td>
</tr>
<tr>
<td>Margaret A. Tempero</td>
<td>University of California - San Francisco</td>
</tr>
<tr>
<td>Sandra L. Wong</td>
<td>University of Michigan</td>
</tr>
</tbody>
</table>

NOTE: Kari Bohlke – ASCO staff

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