

# HOPA NEWS

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Hematology/Oncology Pharmacy  
Association Newsletter

## Current Practices in the Management of Venous Thromboembolism *A Survey of the HOPA Membership and General Medicine Pharmacists*

A concern for all healthcare providers in oncology, including pharmacists, is the high risk that their patients have for venous thromboembolism (VTE). Compared to non-cancer patients, cancer patients have an approximately 4-fold increased risk of a first venous thromboembolism (VTE)<sup>1</sup> and a 2-fold higher rate of VTE recurrence.<sup>2</sup> This increased risk can be associated with grave consequences, with the occurrence of VTE being thought to increase the likelihood of death for cancer patients by 2- to 8-fold.<sup>3-7</sup>

Oncology pharmacists are faced with a complex challenge when managing VTE, given the many confounding factors in the treatment of cancer patients and, until recently, the lack of consensus guidelines. Over the past few years, several national guidelines have been developed for the treatment and prevention of VTEs, including those from the American College of Chest Physicians (CHEST) and the American Society of Health-System Pharmacists (ASHP).<sup>8,9</sup> However, few guidelines have focused on the management of VTE in cancer patients until the release of the National Cancer Center Network (NCCN) guidelines in March 2006.<sup>10</sup> With the development of the NCCN guidelines, oncology pharmacists have an important new tool at their disposal but more work is still needed to ensure that all pharmacists treating cancer patients are fully aware of optimal management techniques for VTE.

### *The HOPA Survey*

HOPA would like to sincerely thank the membership for an outstanding response to the survey on VTE management practices sent in mid-September of 2006. Of the 800 surveys that were sent out, over 100 HOPA members responded (13% response rate), demonstrating the commitment of oncology pharmacists to continually assessing and improving patient care. Some of the key results of the survey are shared below with the hope that they will help to set the baseline from which we can all continue to improve VTE management.

The greatest percentage of responders (42%) reported that their primary practice site was an academic institution, while 16% reported a community hospital, 11% a community oncology center, 11% an NCCN center, and 9% a private office or clinic. The majority of respondents (68%) reported that their primary role was as a clinical pharmacist, with another 22% reporting that they were a director, clinical coordinator, or staff pharmacist. When asked whether their primary practice sites currently have VTE prophylaxis guidelines in place, 55% of respondents said they did not.

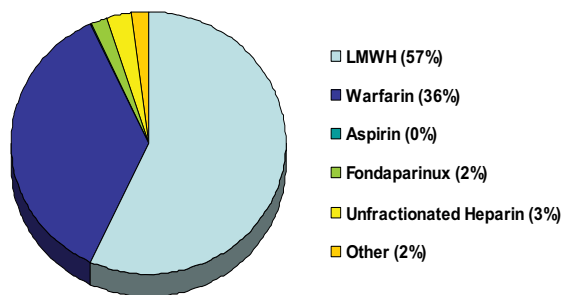
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## VTE Therapies

The most commonly used pharmacologic therapy for VTE prophylaxis was reported as being low molecular weight heparin (LMWH), followed by warfarin, unfractionated heparin, aspirin, and fondaparinux. Nonpharmacologic therapies were also reported as being used in some patients, including graduated compression stockings, intermittent pneumatic compression devices, and the venous foot pump. In patients who have a history of deep vein thrombosis or pulmonary embolism, the majority of respondents (57%) said that they would use low molecular weight heparin (Figure 1). As expected, the survey confirmed the important role that oncology pharmacists play in the management of cancer patients, with 28% reporting that they are sometimes involved in VTE risk assessment, 37% reporting that they are sometimes involved in initiating VTE prophylaxis, and 37% reporting that they are mostly in charge of monitoring therapy (Table 1).

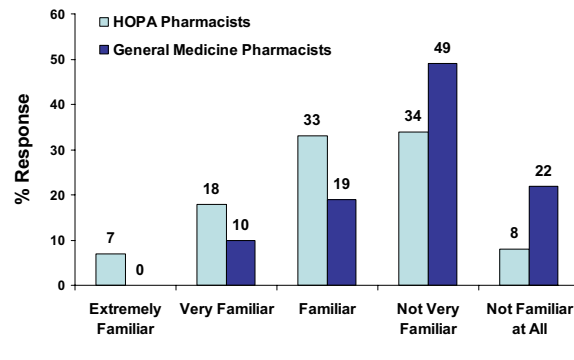
**Figure 1.** In patients who have a history of a DVT/PE, what is the agent of choice [at your institution] for prophylaxis?



## Guidelines

The HOPA survey indicated that despite the potentially positive impact of the NCCN 2006 guidelines on the management of VTE in cancer patients, many oncology pharmacists are still unaware of these guidelines. Of the 105 oncology pharmacists who responded to the survey, 43 (42%) reported that they were not very familiar or not at all familiar with the new guidelines (Figure 2), nearly 6 months after their initial release (the NCCN has since released a second, revised version of the guidelines, in October 2006<sup>11</sup>). Furthermore, the survey indicated that in those institutions in which VTE prophylaxis guidelines are in place, only 25% are currently using the NCCN guidelines. In contrast, the oncology pharmacists reported that over 70% of their institutions are using the CHEST guidelines, institutional guidelines, or a combination of both.

**Figure 2.** How familiar are you with the new NCCN guidelines on VTE prophylaxis for patients with cancer?



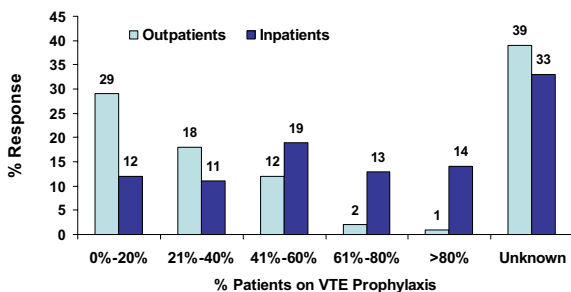
**Table 1.** How often do pharmacists at your institution do the following?

	All the Time	Most of the Time	Some of the Time	Rarely	Never
Screen Patients for Risk of VTE	5%	24%	28%	27%	16%
Recommend VTE Prophylaxis for Patients at Risk	9%	30%	38%	16%	7%
Initiate VTE Prophylaxis	8%	18%	37%	21%	17%
Monitor Therapy	23%	37%	23%	12%	6%

### VTE Prophylaxis

Results from the HOPA survey also indicate that institutions may not always be optimizing VTE management in their cancer patients. Although the NCCN guidelines recommend VTE prophylaxis for all hospitalized cancer patients who do not have contraindications to anticoagulation therapy, only 14% of the oncology pharmacists reported that greater than 80% of their inpatients are receiving prophylaxis (Figure 3). The survey indicated that the percentage of outpatients on VTE prophylaxis was even lower than that for inpatients, with only 1% of oncology pharmacists reporting that 80% or more of their outpatients were on prophylaxis and 29% reporting that 0%-20% of their outpatients were on prophylaxis (Figure 3). On a related topic, 55% of respondents said that their institution did not have a protocol for transitioning VTE prophylaxis from an inpatient setting to an outpatient setting.

**Figure 3.** What percentage of outpatients/inpatients in your practice are on VTE prophylaxis?

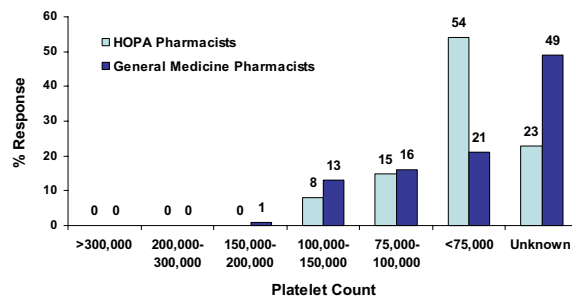


### Heparin-Induced Thrombocytopenia

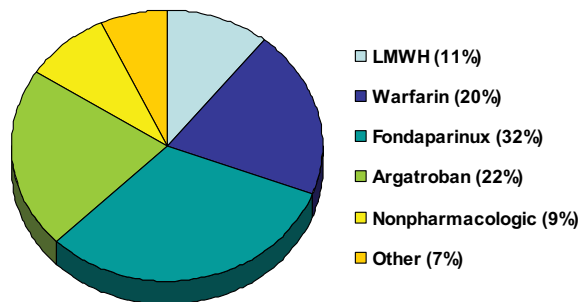
Survey responders reported being apprehensive about the side effects of VTE therapy, in particular heparin-induced thrombocytopenia (HIT), with 53% reporting being “concerned” and 23% reporting being “very or extremely concerned.” Despite this concern, over 20% of oncology pharmacists reported that they did not know at what platelet count they should suspend or avoid initiating anticoagulant therapy (Figure 4) and 32% did not know how often the platelet count should be checked in patients receiving VTE prophylaxis. For those pharmacists who did report an answer, the greatest percentage of responders said that they would suspend or avoid initiating anticoagulant therapy at a platelet count of <75,000 (54%) and that they would

check platelet counts weekly (39%). When asked what prophylaxis treatment they would choose for a patient who had previously experienced HIT, the highest percentage of respondents (32%) said fondaparinux, followed by argatroban, warfarin, low molecular weight heparin, and non-pharmacologic measures (Figure 5).

**Figure 4.** In oncology patients, at what platelet count do you suspend or avoid initiating anticoagulant therapy?



**Figure 5.** When prophylaxing patients who have previously experienced HIT, what is your treatment of choice?



### General Medicine Pharmacists Survey

As a point of comparison to the HOPA survey, a separate survey was sent to 1,867 pharmacists in the general medicine practice setting, which yielded 83 responses (4% response rate). Overall, responses were similar between the surveys sent to oncology versus general medicine pharmacists, although there were some distinctions worth noting. In contrast to the HOPA survey, where the majority of respondents reported that they practiced in an academic hospital, the greatest percentage of general medicine pharmacists said that their primary practice site was a community hospital (48%), followed by an academic institution and a private office or clinic, among other types of sites.

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Perhaps not surprisingly, a greater percentage of the general medicine pharmacists reported that they were not very familiar or not at all familiar with the NCCN guidelines (**Figure 2**), and a higher percentage reported that they did not know at what platelet count they should suspend or avoid initiating anticoagulant therapy in an oncology patient (**Figure 4**). As also might be expected, the majority of pharmacists in general medicine practice reported that primary care physicians had responsibility for screening patients at risk for VTE and making sure they received prophylactic therapy, while respondents in the HOPA survey said that a hematologist or oncologist had primary responsibility for these two roles. Interestingly, more general medicine pharmacists reported that their primary practice site had VTE prophylaxis guidelines in place compared to the HOPA pharmacists (65% vs 45%, respectively).

Institutions nationwide are undoubtedly doing an excellent job of treating their cancer patients, although the HOPA survey results suggest that VTE management could be further optimized to maximize patient care. More education is needed on the importance of VTE prophylaxis, the new NCCN guidelines, and proper HIT management, among other issues. In support of this conclusion, 57% of oncology pharmacists interviewed said that it would be extremely useful to have a “best practices in VTE prophylaxis for oncology patients.”

In the near future, be on the lookout for a Request for Applications in which you will be asked to describe your own institution’s VTE management practices. The top management practices will be selected for a roundtable discussion and development of best practices, which will then be disseminated to the HOPA membership. With your continued involvement, oncology pharmacists nationwide will soon have another new tool for improving VTE management!

### *Sunitinib Review (Sutent<sup>®</sup>, Pfizer, Inc.)*

**Priti N. Patel, PharmD, BCPS**

On January 26, 2006, the US Food and Drug Administration (FDA) approved sunitinib, SU11248, from Pfizer, Inc. Sunitinib is indicated for treatment of gastrointestinal stromal tumor (GIST) after disease progression or intolerance to imatinib mesylate and for

treatment of advanced renal cell carcinoma (RCC). Sunitinib is an oral multikinase inhibitor that inhibits platelet-derived growth factor receptors  $\alpha$  and  $\beta$ , vascular endothelial growth factor receptors 1-3, and other tyrosine kinases.

The efficacy and safety of sunitinib in the treatment of GIST was evaluated in a randomized, double-blind, placebo-controlled, international trial of patients with GIST who had disease progression following treatment with imatinib or who were intolerant to imatinib. The primary objective was to compare time to tumor progression (TTP) in patients receiving sunitinib or placebo, in addition to supportive care. Patients were randomized in a 2:1 ratio to receive either sunitinib 50 mg or placebo once daily for 4 weeks followed by 2 weeks off. Of the 312 intent-to-treat patients, 207 received sunitinib and 105 received placebo. Patients receiving sunitinib had a median TTP of 27.3 weeks, as compared to 6.4 weeks in the placebo group (hazard ratio 0.33; 95% confidence interval 0.23-0.47;  $p < 0.0001$ ). Progression-free survival was 24.1 weeks in the sunitinib group, vs. 6.0 weeks in the placebo group (HR 0.33; 95% CI 0.24-0.47;  $p < 0.0001$ ).

The efficacy of sunitinib as second-line treatment of advanced RCC was studied in an open-label, single-arm multicenter trial of 106 patients with metastatic clear-cell RCC that had progressed despite previous cytokine therapy. Patients were given 6-week cycles of sunitinib 50 mg orally daily for 4 weeks, followed by 2 weeks off. The primary outcome measure was overall objective response rate. Thirty-six patients had partial response (34%; 95% CI 25%-44%). Thirty patients (29%) had stable disease for  $\geq 3$  months. The median progression-free survival was 8.3 months (95% CI 7.8-14.5 months). Approval for this indication was based on the partial response rate and duration of response from this trial. No randomized trials demonstrating increased survival or improvement of disease symptoms in RCC have been conducted.

Patients with concomitant cardiovascular conditions, including severe/unstable angina, coronary or peripheral artery bypass graft, symptomatic congestive heart failure (CHF), cerebrovascular accident, transient ischemic attack, or pulmonary embolism should be carefully monitored for clinical signs and

symptoms of CHF while receiving sunitinib. Left ventricular ejection fraction (LVEF) should be monitored at baseline and periodically in these patients. A baseline LVEF may be considered in patients without previous cardiac risk factors.

Tumor-related hemorrhage has occurred in sunitinib studies in patients with GIST. Hypertension has also been seen and should be treated as needed. Severe hypertension may require temporary discontinuation of sunitinib until blood pressure is controlled. Adrenal insufficiency has been seen in sunitinib studies. Patients who experience stress such as surgery, trauma, or severe infection should be monitored for adrenal insufficiency. A complete blood count and serum chemistries should be performed at the start of each cycle. Sunitinib is pregnancy category D so women of childbearing potential should avoid becoming pregnant while receiving sunitinib. In addition, women should be advised to avoid breastfeeding while receiving sunitinib. The most common adverse events seen in the trial of patients with RCC included fatigue, diarrhea, dyspepsia, hypertension, hand-foot syndrome, nausea, stomatitis, anorexia, mucosal inflammation, vomiting, dysgeusia, extremity pain, and rash. The most common laboratory abnormalities were neutropenia, increased lipase, anemia, and thrombocytopenia. Patients should be warned that skin discoloration due to the yellow color of the drug may occur.

For treatment of GIST and advanced RCC, sunitinib should be given as 50 mg orally once daily for 4 weeks followed by 2 weeks off. Sunitinib can be taken with or without food. Since sunitinib is primarily metabolized by CYP3A4, drugs that either inhibit or induce CYP3A4 will likely interact with sunitinib. A dosage reduction down to a minimum of 37.5 mg daily may be considered for patients on strong CYP3A4 inhibitors, such as ketoconazole. Conversely, the dosage may be increased to a maximum of 87.5 mg daily for patients on CYP3A4 inducers, such as rifampin. St. John's wort must not be taken concomitantly with sunitinib since it may decrease plasma concentrations of sunitinib unpredictably. Sunitinib is available as 12.5 mg, 25 mg, and 50 mg capsules.

Sunitinib has not been studied in patients with impaired hepatic or renal function. In addition,

sunitinib has not been studied in pediatric patients. Additional information regarding sunitinib may be obtained from the Sutent package insert.

### *Outpatient Issues Regarding Oral Targeted Therapy*

**Sheetal Sheth, PharmD, BCOP**  
**Tam Bui, PharmD**

Targeted therapy is an exciting venue for treatment of various cancers. It provides targeted action towards destruction of cancer cells without causing the debilitating adverse effects of traditional chemotherapy. The convenience of oral dosing also allows for ease of administration and treatment at home. Yet, the cost of targeted therapy drugs can be quite significant and obtaining them can be a time-consuming effort, not only for the healthcare professional but also for the patient. Such treatments include but are not limited to erlotinib (Tarceva®), sorafenib (Nexavar®) and sunitinib (Sutent®). The respective AWP for each drug is \$3,350, \$5,200 and \$7,480 for a month's supply. Therefore, assistance programs have been developed by drug companies to aid patients in acquiring these novel agents; however, each program does have its limitations.

Genentech sponsors a drug assistance program for erlotinib called Single Point of Contact® (SPOC). SPOC can be reached at 888-249-4918 or [www.tarceva.com](http://www.tarceva.com). SPOC assists patients in confirming coverage, attaining reimbursement, and helping with claim appeals. This program directly connects the patient to a SPOC representative who prompts the patient to provide some basic demographic information along with their insurance information either verbally or via fax. After SPOC attains the patient information, the turnaround time for a response can take up to 5 business days. SPOC will then contact whoever initiated the request with the outcome. For example, if the doctor's clinic calls in the request, then 5 business days later SPOC will call the clinic with the result. It is then the clinic's responsibility to communicate the outcome to the patient. This process involves several variables that need to be in place for everyone to receive the appropriate information. Another program, Genetech Access to Care Foundation, is available to patients who have a minimal income (<\$75,000) and no prescription insurance. This program offers to mail erlotinib

directly to the patients' home. On the other hand, those patients who have a discount prescription plan are in a difficult situation. Often, they exceed the coverage bracket for financial assistance but are unable to pay for their monthly co-payments (co-pays). Other alternatives must then be investigated.

Pfizer Oncology provides FirstRESOURCE® as sunitinib's drug assistance program, which can be reached at 877-744-5675 or [www.sutent.com](http://www.sutent.com). This program shares similar objectives as SPOC. It essentially provides drug free of charge to limited-income patients who belong to the respective state indigent program. Once the completed enrollment form is faxed to FirstRESOURCE®, Pfizer will then deliver sunitinib to the patient within 2-3 business days. However, the process is not as simple for patients with only discount prescription plans. Pfizer is willing to screen these patients for assistance eligibility but the response can take up to 14 days. The long wait can be frustrating to patients, resulting in numerous phone calls to the clinic. Furthermore, the eligibility is highly dependent on the patient's annual income. If the patient's income exceeds the limit determined by Pfizer, the patient is responsible for fulfilling the requested co-pay entirely out-of-pocket. A similar situation exists for patients with Medicare's gap coverage (also referred to as "doughnut-hole" coverage). There is no financial assistance to help with the expensive co-pay.

Sorafenib's assistance program is the REACH SM Program at 866-639-2827 or [www.nexavar.com](http://www.nexavar.com). It provides reimbursement information for and assists patients in obtaining sorafenib. The program is comparable to those offered by erlotinib and sunitinib for the indigent and Medicare patients. The novel approach that REACH provides is seeking financial assistance through local chapter organizations (eg, the National Kidney Foundation) for patients with substantial co-pays; however, this response can take up to 4 weeks.

The financial repercussions of utilizing these therapies can be enormous for patients. All variables need to be factored in prior to the final decision-making process. Gone are the days where we were fairly certain that many patients had coverage for intravenous chemotherapeutic agents and here are the times where so much more investigation needs to be conducted prior to commencing a therapy. In addition, these

innovative treatments also possess adverse effect profiles (ie, new-onset hypertension, venous thromboembolism, etc) requiring treatment with additional supportive care medications. In the end, many new medications may provide distinct treatment advantages, although the total cost of care can be quite substantial for the patient.

### References

1. Heit JA, Silverstein MD, Mohr DN, et al. Risk factors for deep vein thrombosis and pulmonary embolism: a population-based case-control study. *Arch Intern Med.* 2000;160:809-815.
2. Rickles FR, Levine MN. Epidemiology of thrombosis in cancer. *Acta Haematol.* 2001;106:6-12.
3. Prandoni P, Lensing AW, Cogo A, et al. The long-term clinical course of acute deep venous thrombosis. *Ann Intern Med.* 1996;125:1-7.
4. Levitan N, Dowlati A, Remick SC, et al. Rates of initial and recurrent thromboembolic disease among patients with malignancy versus those without malignancy. Risk analysis using Medicare claims data. *Medicine (Baltimore).* 1999;78:285-291.
5. Sorensen HT, Mellekjær L, Olsen JH, Baron JA. Prognosis of cancers associated with venous thromboembolism. *N Engl J Med.* 2000;343:1846-1850.
6. Heit JA, Silverstein MD, Mohr DN, et al. Predictors of survival after deep vein thrombosis and pulmonary embolism: a population-based, cohort study. *Arch Intern Med.* 1999;159:445-453.
7. Martino MA, Williamson E, Siegfried S, et al. Diagnosing pulmonary embolism: experience with spiral CT pulmonary angiography in gynecologic oncology. *Gynecol Oncol.* 2005;98:289-293.
8. Geerts WH, Pineo GF, Heit JA, et al. Prevention of venous thromboembolism: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. *Chest.* 2004;126:338S-400S.
9. ASHP Commission on Therapeutics. ASHP therapeutic position statement on the use of low-molecular-weight heparins for adult outpatient treatment of acute deep-vein thrombosis. *Am J Health Syst Pharm.* 2004;61:1950-1955.
10. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology: Venous Thromboembolic Disease - V.1.2006.
11. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology: Venous Thromboembolic Disease - V.2.2006. Available at: [www.nccn.org/professionals/physician\\_gls/PDF/vte.pdf](http://www.nccn.org/professionals/physician_gls/PDF/vte.pdf). Accessed Dec 7, 2006.

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