



Key ASH Presentations
Issue 5, 2012

Incidence of Venous Thromboembolism in Patients with Cancer

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CME INFORMATION

OVERVIEW OF ACTIVITY

The annual American Society of Hematology (ASH) meeting is unmatched in its importance with regard to advancements in hematologic cancer and related disorders. It is targeted by many members of the clinical research community as the optimal forum in which to unveil new clinical data. This creates an environment each year in which published results and new information lead to the emergence of many new therapeutic agents and changes in the indications for existing treatments across virtually all malignant and benign hematologic disorders. As online access to posters and plenary presentations is not currently available, a need exists for additional resources to distill the information presented at the ASH annual meeting for those clinicians unable to attend but desiring to remain up to date on the new data released there. To bridge the gap between research and patient care, this CME activity will deliver a serial review of the most important emerging data sets from the latest ASH meeting, including expert perspectives on how these new evidence-based concepts can be applied to routine clinical care. This activity will assist medical oncologists, hematologists and hematology-oncology fellows in the formulation of optimal clinical management strategies and the timely application of new research findings to best-practice patient care.

LEARNING OBJECTIVES

- Assess the benefit-risk profile of the novel ultra-low-molecular-weight anticoagulant semuloparin for the treatment of venous thromboembolism in patients with locally advanced or metastatic cancer.
- Evaluate the efficacy and safety data with anticoagulant therapy for patients with deep vein thrombosis and venous thromboembolism, and incorporate this information into your personal therapeutic algorithm.
- Develop an understanding of the incidence and risk factors for venous thrombosis and venous thromboembolism, and be able to counsel patients with newly diagnosed or recurrent cancer about the appropriate prophylactic treatments available.

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FACULTY — The following faculty (and their spouses/partners) reported real or apparent conflicts of interest, which have been resolved through a conflict of interest resolution process:

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This activity is supported by educational grants from Allos Therapeutics, Celgene Corporation, Genentech BioOncology/ Biogen Idec, Incyte Corporation, Millennium: The Takeda Oncology Company, Onyx Pharmaceuticals Inc, Sanofi and Seattle Genetics.

Last review date: February 2012
Expiration date: February 2013

To go directly to slides and commentary for this issue, [click here](#).

While a bunch of important ASH papers this year focused on prevention and treatment of venous thromboembolism (VTE), perhaps the most clinically relevant data set was a follow-up from the Phase III SAVE-ONCO study initially presented at ASCO and published on February 16th in the *New England Journal*. This landmark randomized trial involving more than 3,200 patients with advanced solid tumors receiving outpatient chemotherapy evaluated the role of the ultra-low-molecular-weight heparin semuloparin versus placebo in preventing VTE.

The editorial that accompanies the *NEJM* publication praises the high quality of this international effort that helped take VTE research in oncology to a new level and provides a much better quantitative understanding of the impact of anticoagulation in patients with cancer where the potential benefits are similar to many oncology interventions, including a number of common chemo regimens. The editorial authors also raise the hope, based on preliminary data, that heparins may have a direct antitumor effect.

To get the inside story on what happened at ASH in this field I chatted with Harvard's VTE maven Dr Ken Bauer, and the data sets listed below are the ones you should know about.

1. **SAVE-ONCO**

During our conversation, Dr Bauer reviewed the impressive hazard reduction in the risk of symptomatic VTE with semuloparin (0.36 — a 64% relative reduction), but he also pointed out that the absolute overall risk in the placebo group was 3.6%, resulting in only about a 2% absolute benefit. This led me to ring up Duke's Dr George, who responded that in unselected (ie, nontrial) populations VTE rates are much higher and since the treatment effect observed in SAVE-ONCO was consistent across risk groups, presumably these patients would benefit even more. Dr George also commented that VTE seems to be associated with significantly increased subsequent mortality in patients with cancer, and in that regard Dr Bauer believes that if we could better quantify risk, patients with greater projected absolute benefit could be identified and receive treatment.

Given that minimal excess bleeding was reported in SAVE-ONCO it's interesting to speculate how much benefit justifies treatment in patients who (as stated in the editorial) "are not bothered much by daily injections." Somewhat similarly, although a number of computer-based VTE risk models are out there, it would be extraordinary if someone could harness the massive quantity of data being generated in trials like SAVE-ONCO to create an Adjuvant! Online-like oncology/VTE model that might include tumor type, stage and specific chemo regimen. This would allow for more precise

estimates of the potential absolute effects of anticoagulation, help doctors and patients make more informed decisions and perhaps lead to a consensus about a level of risk that requires treatment, similar to the 20% bar for risk of neutropenic fever and the preemptive use of growth factors.

2. VTE in the inpatient versus outpatient oncology setting; risk assessment model (RAM) for medical inpatients

At ASH, Dr Alok Khorana presented an [observational retrospective study](#) based on insurance claims demonstrating that more than three quarters of VTE cases in patients with cancer occur in the outpatient setting. Interestingly, Dr Khorana previously published data suggesting that only about half of oncology patients are aware of their increased risk of VTE and when this is explained, many are interested in prevention. [A related ASH paper](#) reported on a RAM that identified 39% of a medical inpatient population as being at high risk for VTE.

3. [Catheter-directed thrombolysis \(CDT\) for acute iliofemoral DVT](#)

Dr Bauer commented that this impressive Phase III randomized trial is perhaps the most methodologically sound study to date to document a reduction in the risk of post-thrombotic syndrome and improved functional outcome with CDT.

4. [Dabigatran versus warfarin in acute VTE \(RE-COVER II study\)](#)

In this Phase II study, the efficacy of dabigatran, an oral anticoagulant from the class of direct thrombin inhibitors, was shown to be noninferior to warfarin with a slightly lower risk of bleeding but a slightly higher incidence rate of acute coronary syndrome. Dr Bauer noted that these findings further contribute to the current challenge associated with selecting from a plethora of new and older agents.

Next on this ASH series: Key data sets in non-Hodgkin lymphoma.

Neil Love, MD

[Research To Practice](#)

Miami, Florida

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Incidence of Venous Thromboembolism in Patients with Cancer

Presentation discussed in this issue

Khorana AA et al. **Higher incidence of venous thromboembolism in the outpatient versus the inpatient setting among US cancer patients.** *Proc ASH* 2011; **Abstract 674**.

Slides from a presentation at ASH 2011 and transcribed comments from a recent interview with Kenneth A Bauer, MD (1/26/12)

Higher Incidence of Venous Thromboembolism (VTE) in the Outpatient versus Inpatient Setting Among Patients with Cancer in the United States

Khorana A et al.
Proc ASH 2011; Abstract 674.

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Background

- Public health efforts to reduce VTE have focused on inpatient thromboprophylaxis, which is proven to be safe and effective.
- VTE is frequent and increasing in the cancer population (*Cancer* 2007;110(10):2339).
- However, cancer care has shifted primarily to outpatient-based therapy.
- Contemporary data regarding the proportion of VTE in the outpatient versus inpatient cancer settings are lacking.
- **Current study objectives:** Determine the proportion of VTE in patients with cancer in the outpatient versus inpatient settings and determine the consequences of VTE in terms of resource utilization and costs.

Khorana A et al. *Proc ASH* 2011;Abstract 674.

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Methods

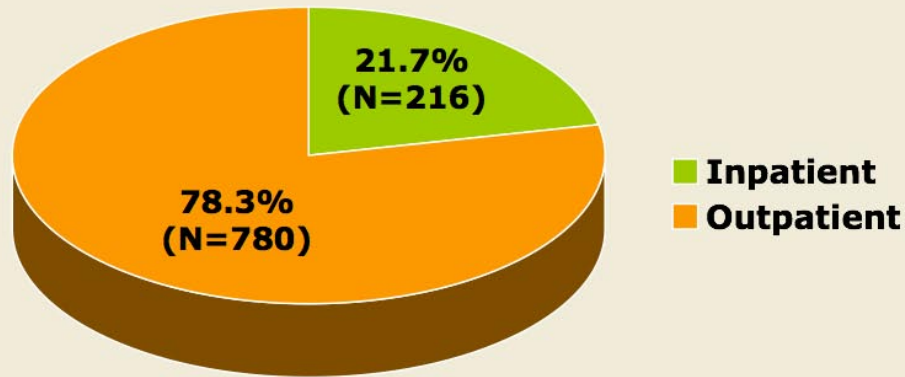
- Observational, retrospective cohort analysis of data extracted from the Premier Perspective™ Database* linked with claims data.
- ICD-9-CM codes were used to identify VTE events, including deep vein thrombosis (DVT) or pulmonary embolism (PE).
- Patients with ≥ 1 inpatient or outpatient claims containing a cancer diagnosis between 2006 and 2008 were included.
- Baseline characteristics of patients were assessed during a 6-month preindex period.
- Demographics, clinical characteristics and cost were assessed.
- Multivariate analyses were conducted to adjust for differences in patient characteristics before and after the index event.

* A deidentified United States hospital clinical and economic database

Khorana A et al. *Proc ASH* 2011;Abstract 674.

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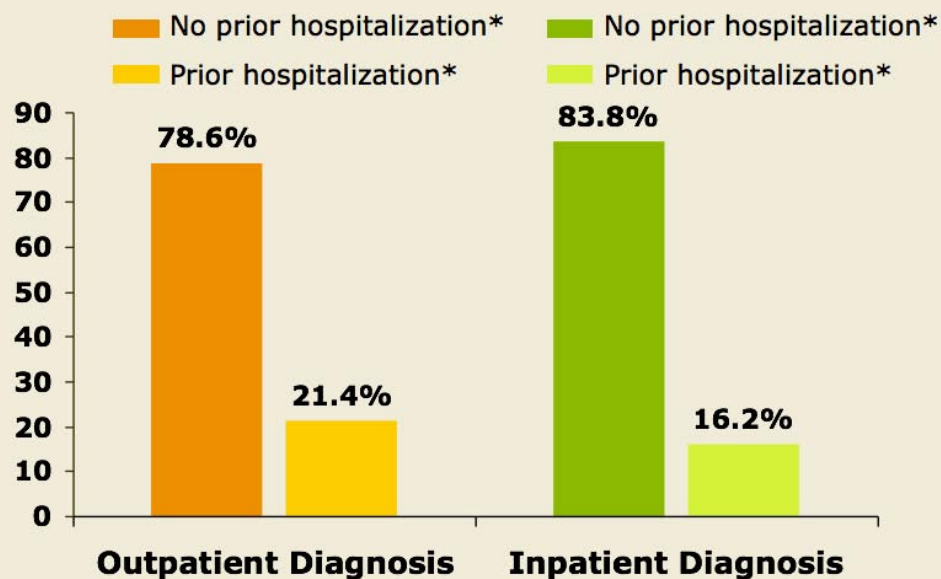
VTE in Cancer Outpatient versus Inpatient



With permission from Khorana A et al. *Proc ASH* 2011;Abstract 674.

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All-Cause Hospitalization Within 30 Days of VTE

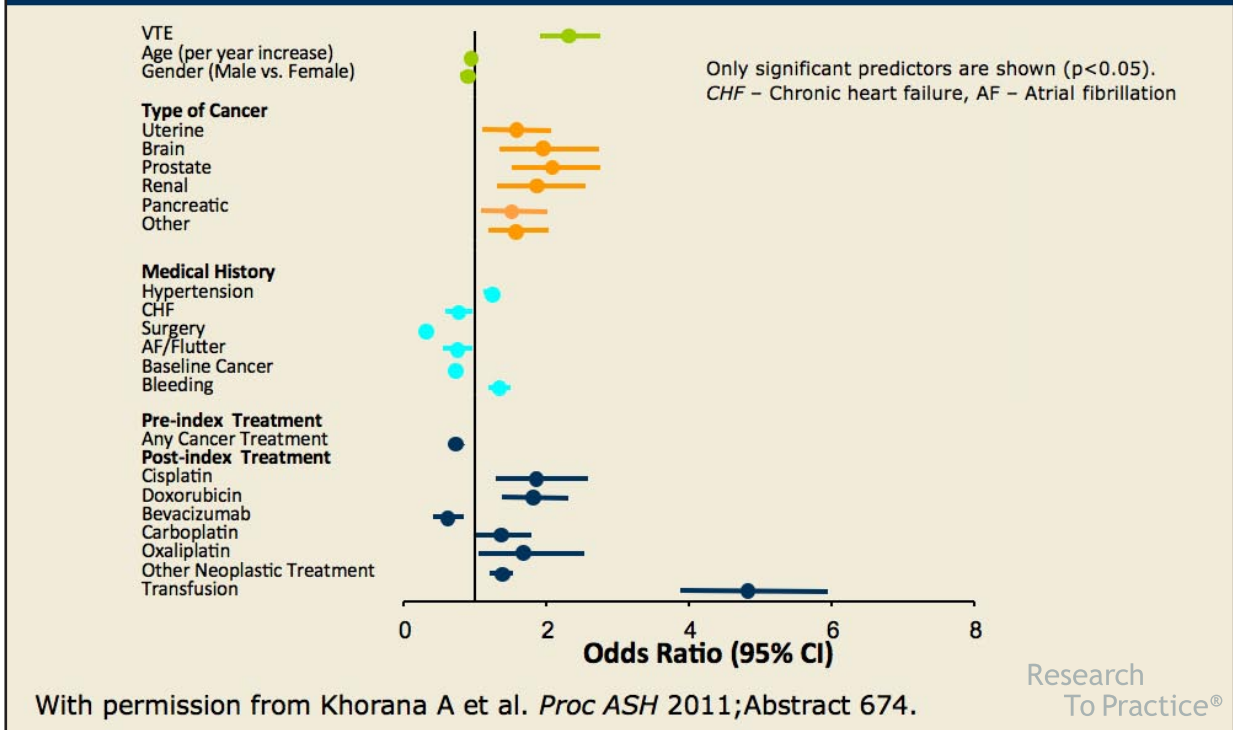


* Within 30 days prior to VTE

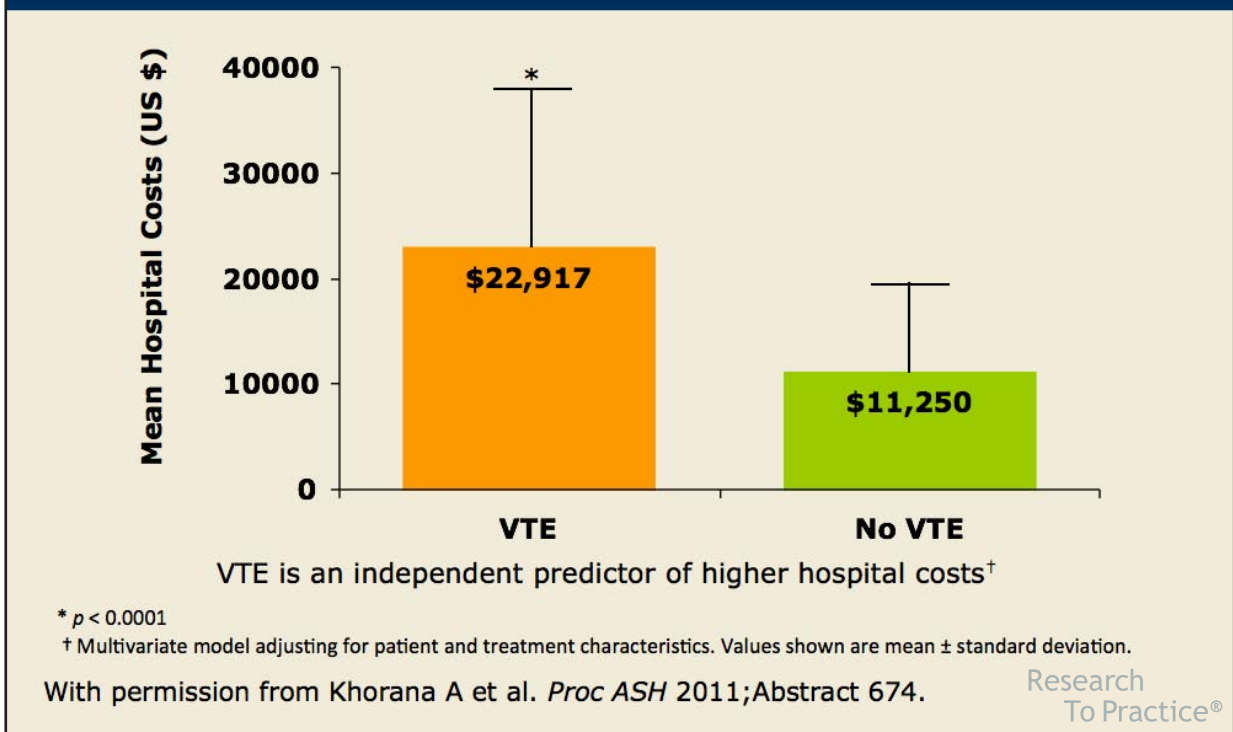
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Predictors of All-Cause Hospitalization



Economic Burden of VTE in Cancer



Author Conclusions

- Over three quarters of all VTE in cancer occurs in the outpatient setting.
- One fifth of outpatients with VTE were recently hospitalized.
- Cancer-associated VTE is associated with hospitalization and increased costs.
- As all data were extracted from an insurance claims database, the study cohort represents a commercially insured population and findings may not be applicable to other populations.
- Public health efforts to reduce the burden of VTE in cancer will need to focus on outpatient (and postdischarge) thromboprophylaxis in patients at high risk.

Khorana A et al. *Proc ASH* 2011;Abstract 674.

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Investigator Commentary: Higher Incidence of VTE in Patients with Cancer in the Outpatient versus Inpatient Settings in the United States

This was a large database study that evaluated the risk of developing VTE for patients with cancer in the outpatient versus the inpatient setting.

The whole area of medical prophylaxis is quite controversial. Some previous studies showed no mortality benefit with heparin in a hospital setting. In this study, about 78% of the patients developed VTE out of the hospital. So it is important to identify the outpatients who are at high risk for VTE. About 21% of the outpatients who developed VTE had been hospitalized in the previous month. So the question is whether using prophylaxis for an extended period after patients leave the hospital can prevent VTE. We know that patients have a major risk of VTE for 90 days after hospitalization.

Interview with Kenneth A Bauer, MD, January 26, 2012

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