



Key ASH Presentations
Issue 5, 2012

Risk Assessment Model for Venous Thrombosis

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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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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Risk Assessment Model for Venous Thrombosis

Presentation discussed in this issue

Zakai N et al. **Development and testing of a risk assessment model for venous thrombosis in medical inpatients: The medical inpatients and thrombosis (MITH) study score.** *Proc ASH 2011*; [Abstract 173](#).

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

Development and Testing of a Risk Assessment Model for Venous Thrombosis in Medical Inpatients: The Medical Inpatients and Thrombosis (MITH) Study Score

Zakai N et al.

Proc ASH 2011; Abstract 173.

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Background

- For hospitalized patients, venous thrombosis (VT) risk assessment and provision of VT prophylaxis are mandated by various governmental organizations such as:
 - The Joint Commission, United States
 - The National Institute for Health and Clinical Excellence, United Kingdom
- No validated VT risk assessment models (RAMs) are available for use with medical inpatients.
- **Current study objective:**
 - Develop a validated RAM that assesses the risk of developing VT in medical inpatients.

Zakai N et al. *Proc ASH* 2011;Abstract 173.

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Study Method

- Between 01/2002 and 06/2009, all cases of VT-complicating medical admissions were:
 - Identified by ICD-9 codes
 - Confirmed by review of medical records at a 500-bed teaching hospital
- Controls without VT (n = 601) were matched to each case (n = 299) in a 2:1 ratio by admission service and admission year.
- VT required positive imaging or autopsy.
- Medical history, comorbidities and the use of VT prophylaxis in cases and controls were assessed by chart review.

Zakai N et al. *Proc ASH* 2011;Abstract 173.

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Study Method (Continued)

- Weighted logistic regression was used to calculate the odds ratio (OR) for VT.
 - The Taylor series method for 95% CI was used to assess mechanical and pharmacologic VT prophylaxis use.
- A point value was assigned to each risk factor.
- A RAM was developed by clinical judgment and sequentially adding risk factors into a multivariate model.
- The 95% CI for the C statistic was used to validate the RAM model.

Zakai N et al. *Proc ASH* 2011;Abstract 173.

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VT Risk Assessment Model* (Abstract Only)

Risk factor	PIC	OR (95% CI)	Points
History of congestive heart failure	5.4%	8.6 (4.1-22.6)	5
History of rheumatologic or ID	1.0%	7.7 (3.3-18.1)	4
Fracture in the past 3 months	1.9%	3.8 (1.6-9.0)	3
History of VT	6.2%	2.7 (1.5-5.0)	2
History of cancer in the past 12 months	17.6%	1.6 (1.1-2.4)	1
Heart rate \geq 100 on admission (OD)	17.0%	2.5 (1.7-3.7)	2
Oxygen saturation $<$ 90%/intubated OD	16.3%	1.9 (1.2-2.9)	1
White cell count \geq 11 OD	29.8%	1.9 (1.2-2.9)	1
Platelet count \geq 350 OD	10.0%	1.9 (1.1-3.1)	1

PIC = prevalence in controls; ID = inflammatory disease

* A point value was assigned to each risk factor based on statistical principles.

- The C statistic for the model was 0.73 (95% CI: 0.70-0.76).

Zakai N et al. *Proc ASH* 2011;Abstract 173.

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RAM Outcomes (Abstract Only)

Rate of VT per 1,000 admissions	95% CI
4.6	3.9-5.4
Probability of VT without VT prophylaxis per 1,000 admissions (score <2)*	95% CI
1.5	1.0-2.3
Probability of VT without VT prophylaxis per 1,000 admissions (score \geq2)*	95% CI
8.8	4.1-18.8
C statistic to validate the developed RAM model	95% CI
0.71	0.68-0.74

* Represents sum of point values for VT risk factors present. Using a cutoff of \geq 2 points as high risk, 79% of cases and 39% of controls were classified as high risk.

Zakai N et al. *Proc ASH* 2011;Abstract 173.

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Author Conclusions

- The internally validated RAM assesses the risk of VT complicating medical admission.
- The score is simple, relies only on information easily known at the time of admission and could be incorporated into an electronic medical record.
- The score allows clinicians to assess VT risk at admission for medical inpatients and to weigh the risks and benefits of pharmacologic VT prophylaxis.
- The RAM will enable further studies to determine optimal VT prevention strategies for medical inpatients.

Zakai N et al. *Proc ASH* 2011;Abstract 173.

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Investigator Commentary: Development and Testing of a Risk Assessment Model for VT in Medical Inpatients

The issues associated with assessing medical patients for the risk of developing VT has controversies brewing about universal prophylaxis for these patients. Identifying patients who have a high risk of developing VT with certitude in addition to determining the patient in need of VT-preventive therapy have been problematic. This study addresses these issues by attempting to develop a risk score for patients potentially at risk for developing VT.

A real knowledge gap exists among many patients in the general population about the problem of venous thromboembolism. The Surgeon General issued a call to action a few years ago to reduce the number of cases of deep vein thrombosis and pulmonary embolism. Once the population becomes more aware of the problems associated with VT, it may be easier to discuss these issues with individual patients.

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