VTE Prevention Across the Continuum: Applications of Clinical Evidence for Extended Prophylaxis from Inpatient to Outpatient Care

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Faculty

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Faculty Disclosures

Dr. Munger has disclosed no relevant financial relationships with any commercial interest.

Learning Objectives

- Quantify the clinical and economic burdens associated with VTE in patients admitted for acute medical illness as well as post-discharge
- Describe the standard of care for VTE prophylaxis in the acute hospitalization and post-discharge care settings
- Evaluate the latest clinical evidence associated with the use of DOACs for the acute and extended prophylaxis of VTE, particularly the implications of newly approved factor Xa inhibitors
- Incorporate risk stratification tools, patient-specific factors, and shared decision-making within the identification of patients who would most benefit from extended VTE prophylaxis
- Lead the interdisciplinary care team in the management of anticoagulant therapy for VTE prophylaxis, ensuring individualized therapeutic selection, patient-centric education and monitoring, and coordinated transitions of care from hospital to outpatient settings

VTE = venous thromboembolism; DOAC = direct oral anticoagulant.

Question: To what extent does pharmacologic prophylaxis reduce the risk of fatal VTE events in hospitalized medical patients?

Audience Response Question

1. 20% RRR
2. 40% RRR
3. 60% RRR
4. 80% RRR

RRR = relative risk reduction.

VTE in Medical Patients Is a Major Public Health Crisis

"Deep vein thrombosis and pulmonary embolism represent a major public health problem, exacting a significant human and economic toll on the nation."

— US Surgeon General (2008)

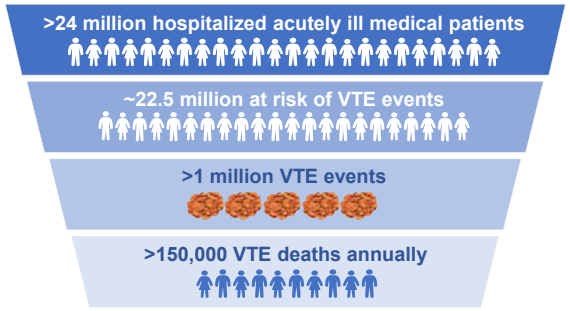
"1 in 4 people worldwide dies of conditions caused by thrombosis. It is a leading cause of global death and disability."

— World Thrombosis Day

Office of the Surgeon General; National Heart, Lung, and Blood Institute. 2008. isth [website]. Know thrombosis: learn & share. http://www.worldthrombosisday.org/issue/thrombosis. Accessed February 1, 2018. ISTH Steering Committee. Thrombosis: a major contributor to the global disease burden. October 9, 2014.

Burden of Illness

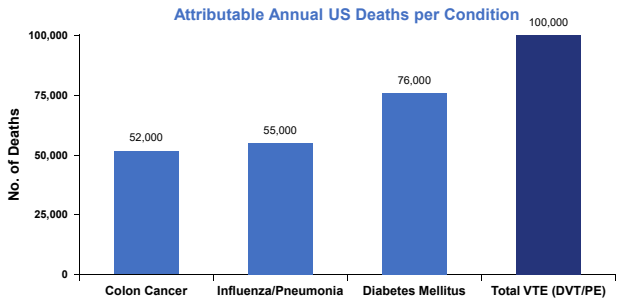
In G7[a] countries, how big is the at-risk population of acutely ill medical patients annually?



[a]G7 countries: Canada, France, Germany, Italy, Japan, the United Kingdom, and the United States.

Cohen AT, et al. *N Engl J Med*. 2016;375:534-544. Roger VL, et al. *Circulation*. 2011;123:e18-e29. Ng TMH, et al. *Circ Heart Fail*. 2010;3(1):165-173. Kelly J, et al. *Stroke*. 2001;32(1):262-267. Tapson VF. *Proc Am Thorac Soc*. 2005;2(1):71-77.

In the United States, Overall VTE Is Deadlier Than Colon Cancer, Diabetes Mellitus, Influenza, and Pneumonia

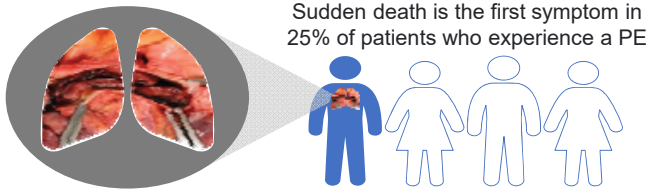


VTE causes ~100,000 confirmed annual deaths in the United States

DVT = deep vein thrombosis; PE = pulmonary embolism.
CDC. Colorectal (colon) cancer. https://www.cdc.gov/cancer/colorectal/statistics. Last updated January 23, 2018. Accessed February 1, 2018. CDC *Health, United States*, 2015. Office of the Surgeon General 2008.

Up to 80% of Fatal VTE Events Occur in Acutely Ill Medical Patients

VTE can be a silent killer: Often the first symptom of a VTE is a fatal PE



Acutely ill medical patients have an 8x higher risk of VTE vs the general population

Huang W. *PloS ONE*. 2015;10(3):e0121429. Futterman LG, et al. *Am J Crit Care*. 2004;13(5):431-436. Office of the Surgeon General and National Heart, Lung, and Blood Institute. *Call to Action to Prevent DVT and PE*. 2008. Beckman MG, et al. *Am J Prev Med*. 2010;38(4 suppl):S495-S501. Kahn SR, et al. *Chest*. 2012;141(2 suppl):e195S-e226S.

Transitions of Care in VTE Research Program (University of Utah)

- **Department of Pharmacotherapy and Thrombosis Service Investigators**
  - **Michael Feehan**, PhD, Research Professor
  - **Dan Witt, PharmD**, Vice Chair & Professor (Clinical)
  - **Ryan Fleming, PharmD**, Manager, Thrombosis Service
  - **Mark Munger, PharmD**, Professor & Associate Dean, College Affairs
  - **Stacy Johnson**, MD, Medical Director, Thrombosis Service
- **2-year program**
  - Initial qualitative interviews with patients
  - National survey
  - Pre- and post-evaluation of patients in Thrombosis Services

Feehan M, et al. *Patient VTE TOC Journey Model*. 2013:1-13.

Background and Objectives

- VTE, including DVT of the lower and upper extremities and PE, is associated with reduced survival, a high rate of recurrence, poorer quality of life, and substantial healthcare costs
- Any interventions that can reduce the risk of VTE recurrence will benefit patients' personal lives, but also benefit society in terms of reduced healthcare costs

Research Objectives

- Primary objective: To build a novel patient-centric statistical model of factors driving success and adversity in VTE care
- Model will ultimately be used to identify potential VTE care intervention targets and then validate the model by implementing targeted VTE care interventions in the University of Utah Health Care (UUHC) Thrombosis Services and measuring associated care outcomes

Feehan M, et al. *Patient VTE TOC Journey Model*. 2013:1-13.

Quantitative Research Design: Patients

- **Online survey of 971 patients with VTE in the United States from May 10, 2016, through July 10, 2016**
  - Before entering the survey, patients were screened online based on the following criteria
    - Aged ≥18 years
    - Experienced at least one VTE event within the past 2 years
    - Not diagnosed with cancer within the past 2 years
  - Quotas for patients with VTE were set to allow adequate representation within subgroups of interest
- **Report based on data from 907 patients after the data set was "cleaned" to remove erroneous responses**

Feehan M, et al. *Patient VTE TOC Journey Model*. 2013:1-13.

Transitions of Care in VTE Research Program (University of Utah)

Patient Characteristics		
Age (years)		52.4±14.4
Gender (M:F %)		M:F 43:57
Race		White: 89% / Black: 7% Asian: 2% / Other: 2%
Comorbidity Index		3.32 ± 2.78
Previous Patient Diagnoses	Anxiety	27%
	Asthma/COPD	16% / 13%
	Depression	28%
	Heart Disease	27%
	Hypertension	46%
	Hypercholesterolemia	38%
DVT/PE/Both		64% / 18% / 18%
# of DVT Episodes/ Lifetime	1	35%
	2	24%
	2+	65%

COPD = chronic obstructive pulmonary disease.
Feehan M, et al. *Patient VTE TOC Journey Model*. 2013:1-13.

High Emotional Impact of VTE

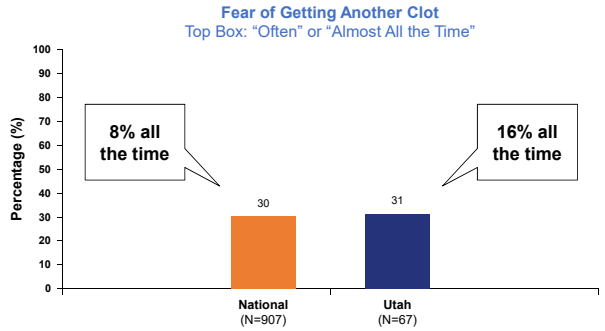
- Extracted themes from 17 qualitative online interviews with patients with VTE across the country in March 2016
- Patient stories highlighted the **emotional impact of VTE** at all stages of the journey from diagnosis to maintenance therapy, and from hospital to home
- Dangerous animals typified life with VTE

*"I was **terrified**. I had almost died the day before; it was **deeply traumatic**"*

*"I have **sought help for stress management**, adjustment due to health changes and **depression**"*

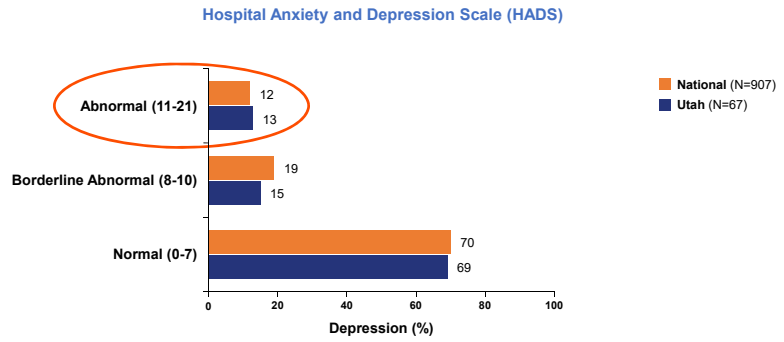
Feehan M, et al. Emotional Impact of Venous Thromboembolism (VTE): A Qualitative Study of Patients' Journeys. *Inside Patient Care*. 2017;5:3.

Patients Fear Future Clots



Feehan M, et al. Emotional Impact of Venous Thromboembolism (VTE): A Qualitative Study of Patients' Journeys. *Inside Patient Care*. 2017;5:3.

More Than 10% Are Currently Depressed



Feehan M, et al. Emotional Impact of Venous Thromboembolism (VTE): A Qualitative Study of Patients' Journeys. *Inside Patient Care*. 2017;5:3.

Emotional Harms Associated with Multiple Factors

- Provisional modeling of the national data showed **emotional harms** (ie, a composite measure of anxiety, depression, emotional distress, or cognitive impairment) were significantly associated ($P<.05$) with:
  - High fear of another clot
  - Poor health literacy
  - Having multiple physical comorbidities
  - Being non-white
  - Younger age
  - Poor health locus of control – Lack of perceived self-control over health
  - Having had a physician make mistakes in the care of VTE
  - Barriers to care (eg, difficulty in paying for healthcare, paying for VTE medications, transportation issues, needing the support of others to obtain care)

Waldron B. Clot Connect [website]. Last updated February 28, 2012. Accessed February 5, 2018.

VTE Has a Substantial Economic Impact[a]

Total VTE medical costs	**$6.7-$9.8 BILLION per year**
Direct medical costs for acute treatment	$11,500-$14,900 per adult patient in 1st year
Costs of VTE treatment and related complications	$17,900-$23,100 per adult patient >1 year[b]

[a]Costs reported in 2014 US dollars (rounded to the nearest $100) based on an incidence-based estimate of 3 published studies. Total annual medical costs based on an estimated 375,000-425,000 newly diagnosed cases per year.
[b]Includes (after the first year) post-thrombotic syndrome, chronic thromboembolic pulmonary hypertension, recurrent VTE, anticoagulation-related adverse drug events.
Grosse SD, et al. *Thromb Res*. 2016;137:3-10.

At-Risk Patients

Most Hospitalized Patients Are Non-Surgical Medical Patients

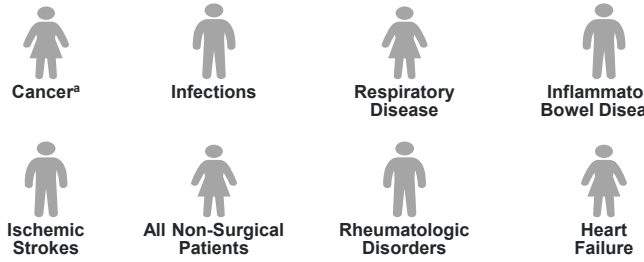
In a multi-national, cross-sectional study of 68,183 hospital patients

Nearly half of all hospitalized medical patients are at risk of VTE

Cohen AT, et al. *Lancet*. 2008;371(9610):387-394.

Who Are Acutely Ill Medical Patients?

IMMOBILITY • HYPERCOAGULABILITY • INFLAMMATION



[a]Cancer requiring primary therapy or therapy for complications.
Di Nisio M, et al. *Drug Des Devel Ther*. 2013;7:973-980.

For Acutely Ill Medical Patients, Immobilization[a] Extends VTE Risk after Discharge

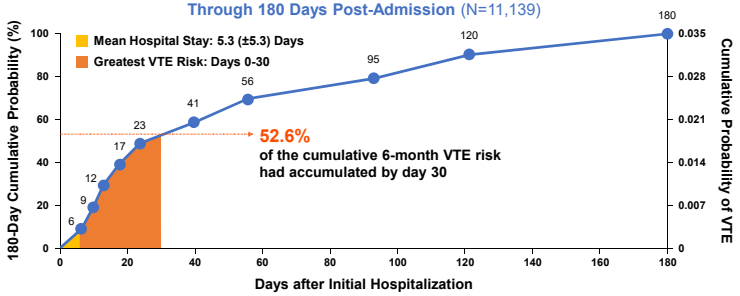
- Immobilization can continue for weeks after hospitalization regardless of post-discharge setting

- Shorter hospital stays lengthen periods of outpatient bed-rest and immobility
- Acute medical illness flare-ups or exacerbations can require re-hospitalization and further immobilization

[a]In clinical studies, immobilization is defined as confinement to bed or to a chair at bedside.
Cohen AT, et al. *N Engl J Med*. 534-544. Rocha AT, et al. *Vasc Health Risk Manage*. 2007;3(4):533-553. Robinson AM. *Ann Longterm Care*. 2013;21(9):28-32. Spencer FA, et al. *Arch Intern Med*. 2007;167(14):1471-1475. Bjóri E, et al. *J Thromb Haemost*. 2016;14(12):2368-2375.

In Hospitalized, Acutely Ill Medical Patients, More Than Half of VTE Events Occur Within 30 Days

Cumulative Risk of VTE in Hospitalized Acutely Ill Medical Patients Through 180 Days Post-Admission (N=11,139)

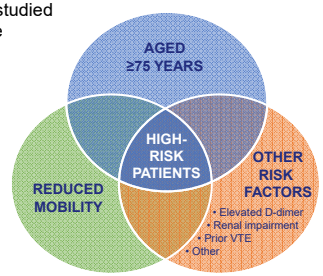


More than half of the cumulative VTE risk occurs within 30 days

Amin AN, et al. *J Hosp Med*. 2012;7(3):231-238.

Effective Extended-Duration VTE Prophylaxis Is Needed for Acutely Ill Medical Patients at High Risk

- Enoxaparin, rivaroxaban, and apixaban were studied as extended-duration VTE prophylaxis in three phase 3 trials
- These trials included patients with common risk factors
  - Aged ≥75 years
  - Reduced mobility
  - Elevated D-dimer
  - Renal impairment
  - Prior VTE
  - Other

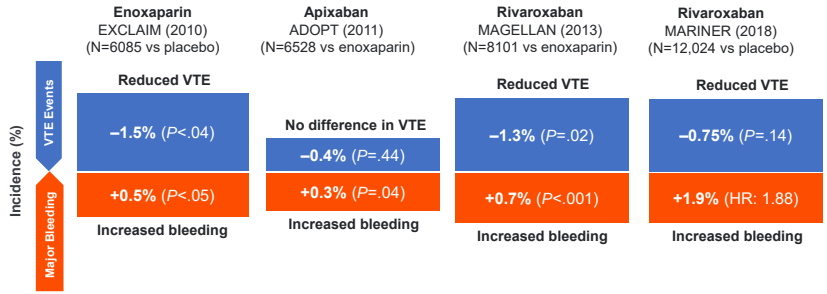


7.7 million US patients at risk of VTE

Cohen AT, et al. *J Thromb Haemost*. 2014;31:473-493. Goldhaber SZ. *N Engl J Med*. 1998;339:93-104. Hull RD. *Ann Intern Med*. 2010;153(1):8-18. Anderson FA, et al. *Am J Hematol*. 2007;82:777-782.

Unmet Need

For Acutely Ill Medical Patients, No Anticoagulant Is Approved for VTE Prevention in the Extended-Duration Setting



No agent demonstrated a compelling net clinical benefit

Hull RD, et al. *Ann Intern Med*. 2010;153(1):8-18. Goldhaber SZ, et al. *N Engl J Med*. 2011;365(23):2167-2177. Cohen AT, et al. *N Engl J Med*. 2013;368(6):513-523. Spyropoulos AC, et al. *N Engl J Med*. August 26, 2018. doi: 10.1056/NEJMoa1805090.

For At-Risk, Hospitalized, Acutely Ill Medical Patients, Guidelines Recommend Only Initial VTE Prophylaxis

- **All major clinical guidelines weigh VTE risk against risk of serious bleeding with treatment**
  - Guidelines recommend an initial short-duration course of pharmacologic prophylaxis (ie, 6-14 days) for acutely ill medical patients with high VTE risk and low bleeding risk
    - Current recommended options in the United States include low-molecular-weight heparin, unfractionated heparin, or fondaparinux
  - Recommendations are informed by the high rate of VTE events and trial data showing a net clinical benefit with in-hospital prophylaxis

Guidelines do not recommend extended-duration prophylaxis for acutely ill medical patients because clinical trials have failed to identify a safe post-discharge therapy

Kahn S, et al. *Chest*. 2012;141(2 suppl):e195S-e226S. Korjian S, et al. *J Cardiovasc Pharmacol Ther*. 2016;21(3):227-232.

Meeting the Need? You Decide

APEX Trial

APEX Trial

OBJECTIVE | PATIENTS | STUDY DESIGN | ENDPOINTS

To demonstrate the safety and efficacy of in-hospital and extended-duration (35-42 days) anticoagulation with betrixaban compared with standard-of-care anticoagulation with enoxaparin (6-14 days) followed by placebo for prevention of VTE in acutely ill medical patients

Cohen AT, et al. *Am Heart J*. 2014;167(3):335-341.

New Oral Anticoagulants (Factor Xa Inhibitors): Pharmacodynamics and Pharmacokinetics

Property	Dabigatran	Rivaroxaban	Apixaban	Edoxaban	Betrixaban
Mechanism of Action	Direct IIa Inhibitor	Direct Xa Inhibitor	Direct Xa Inhibitor	Direct Xa Inhibitor	Direct Xa Inhibitor
Bioavailability	6%-7%	80%	50%	62%	34%
T_{max}	1.5 hours	2-4 hours	2-3 hours	1-2 hours	3-4 hours
$T_{½}$	12-14 hours	9-13 hours	8-15 hours	8-11 hours	19-27 hours
Hepatic Metabolism	No	Yes	Yes	Yes	No
Drug Interactions	P-gp	CYP3A4	CYP3A4	P-gp	P-gp
Protein Binding	35%	90%	87%	55%	60%
Dialyzable	Yes	No	No	No	No
Measurement	ECT, TT, aPTT	Anti-Xa, PT	Anti-Xa, dPT	Anti-Xa, PT	Anti-Xa, PT
Renal Elimination	80%	35%	25%	40%	11%
Renal Dosing	Yes	Yes	No?	Yes	Yes
Antidote	No	No	No	No	No

FDA [website]. Drugs@FDA approved drug products. https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&applno=208383. Accessed February 1, 2018.

Comparison of Agents

	Warfarin	Dabigatran	Rivaroxaban	Apixaban	Betrixaban
Special Instructions	None	Do not chew, break open capsules - ↑ bioavailabiity by 75% Keep in original bottle and tightly capped Must use within 4 months of opening	None	None	None
Pre-Procedure Dosing	Stop 5-6 days prior procedure May need bridging	Skip 2-8 doses depending on procedure and renal function No need for bridging	Stop >24 hours before OR and other interventions	Stop 24-48 hours before elective OR and other interventions	Stop 72 hours before elective OR and other interventions
Diet Considerations	Consistent intake of Vitamin K-containing foods	None	Take with food	None	Take with food at same time each day
Cost	$4/month + $20/INR (Annual cost ≈$1000)	$200-400/month Patient Assistance Program (Annual cost ≈$2400-$4800)	$299/month (AWP) CarePath™ Patient Support and Assistance Program (Annual cost ≈$3600)	$299/month (AWP) Eliquis® 360 Support Patient Support and Assistance Program (Annual cost ≈$3600)	$15/40 or 80 mg (AWP) CoverMyMeds™ Program Patient Support and co-pay offset cards (42-day cost ≈$610)

Note: Betrixaban is only used for 42 days; therefore, annual cost is not appropriate from the cost basis.
INR = international normalized ratio; AWP = average wholesale price.
FDA [website]. Drugs@FDA approved drug products. https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&applno=208383. Accessed February 1, 2018.

APEX Trial Inclusion Criteria

OBJECTIVE | **PATIENTS INCLUDED** | STUDY DESIGN | ENDPOINTS

HOSPITALIZED FOR ACUTE MEDICAL ILLNESS

Heart Failure, Respiratory Failure, Infectious Disease, Rheumatic Disease, or Ischemic Stroke

EXPECTED MODERATE / SEVERE IMMOBILITY

Age and Additional Risk Factors			
≥75 Years	60 to 74 Years	40 to 59 Years	Additional Risk Factors
Eligible	2 additional risk factors **OR** D-dimer ≥2x ULN	History of VTE **OR** History of cancer + 1 additional risk factor **OR** D-dimer ≥2x ULN	• Previous VTE or superficial vein thrombosis • History of NYHA class III or IV HF • Concomitant acute infection • Obesity (BMI >35) • History of cancer • Inherited or acquired thrombophilia • Current use of erythropoiesis-stimulating agent • Hormone therapy

ULN = upper limit of normal; NYHA = New York Heart Association; HF = heart failure; BMI = body-mass index.
Cohen AT, et al. *Am Heart J*. 2014;167(3):335-341.

APEX Trial Exclusion Criteria

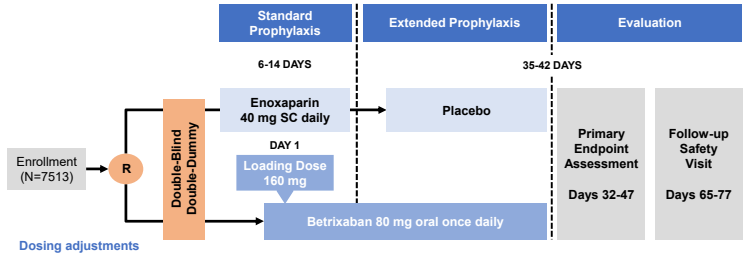
OBJECTIVE | **PATIENTS EXCLUDED** | STUDY DESIGN | ENDPOINTS

- End-stage renal disease with CrCl <15 mL/min, or requiring dialysis
  - APEX is the first extended thromboprophylaxis trial to enroll patients with CrCl <30 mL/min
- Anticipated need for prolonged anticoagulation
- Current intake of dual antiplatelet therapy
- Anticipated major surgery
- History of clinically significant bleeding within 6 months prior to enrollment
- History of intracranial bleeding, head trauma, or known intracranial lesions
- History of significant gastrointestinal, pulmonary, or genitourinary bleeding, ongoing chronic peptic ulcer disease, or ongoing or acute gastritis within 2 years prior to enrollment
- Hemoglobin <9.5 g/dL or unstable/declining hemoglobin

CrCl = creatinine clearance.
Cohen AT, et al. *N Engl J Med*. 2016;375(6):534-544. Cohen AT, et al. *Am Heart J*. 2014;167(3):335-341.

APEX Trial

OBJECTIVE | PATIENTS | **STUDY DESIGN** | ENDPOINTS



Dosing adjustments

- In severe renal insufficiency (CrCl 15 to <30 mL/min): Betrixaban 40 mg (80-mg loading dose); enoxaparin 20 mg SC daily
- In betrixaban patients taking concomitant strong P-gp inhibitors: Betrixaban 40 mg (80-mg loading dose)

P-gp = P-glycoprotein; SC = subcutaneous.
FDA [website]. Drugs@FDA approved drug products. https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&appIno=208383. Accessed February 1, 2018. Cohen AT, et al. *Am Heart J*. 2014;167(3):335-341. Cohen AT, et al. *N Engl J Med*. 2016;375(6):534-544.

APEX Trial (cont)

OBJECTIVE | PATIENTS | STUDY DESIGN | **ENDPOINTS**

Primary Efficacy Endpoint

- Composite of VTE-related death, non-fatal PE, asymptomatic proximal DVT, or symptomatic DVT

Secondary Efficacy Endpoint

- Composite of symptomatic VTE (VTE-related death, non-fatal PE, or symptomatic DVT) through day 42

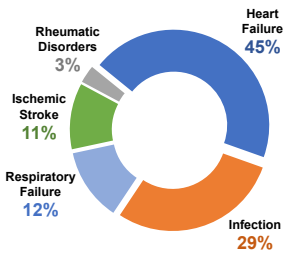
Primary Safety Endpoint

- Occurrence of major bleeding through 7 days after discontinuation of all study medication

Cohen AT, et al. *Am Heart J*. 2014;167(3):335-341.

APEX Patient Characteristics at Baseline

Primary Acute Medical Illness



Additional VTE Risk Factors

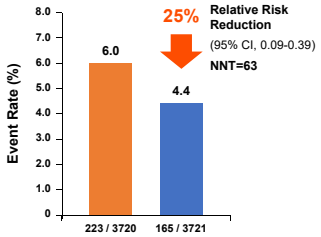
	% of Patients
Aged ≥75 years	68
D-dimer ≥2x ULN	62
History of NYHA class III or IV heart failure	23
Obesity (BMI >35)	19
Severe varicosities	19
Concurrent acute infection	16
History of cancer	12
Previous VTE	8
Hormone replacement therapy	1.0
Inherited or acquired thrombophilia	0.1

FDA [website]. Drugs@FDA approved drug products. https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&applno=208383. Accessed February 1, 2018. Cohen AT, et al. *N Engl J Med*. 2016;375(6):534-544.

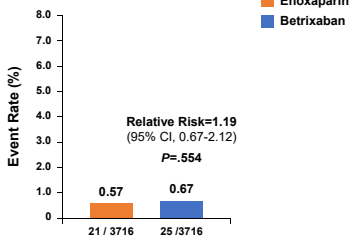
Primary Efficacy and Safety Endpoint

80-mg & 40-mg doses

PRIMARY EFFICACY OUTCOME
Total VTE or VTE-Related Death
mITT Population



PRIMARY SAFETY OUTCOME
Major Bleeding
Safety Population

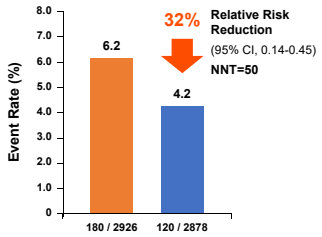


mITT = modified intent to treat; NNT = number needed to treat.
FDA [website]. Drugs@FDA approved drug products. https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&applno=208383. Accessed February 1, 2018. Cohen AT, et al. *N Engl J Med*. 2016;375(6):534-544.

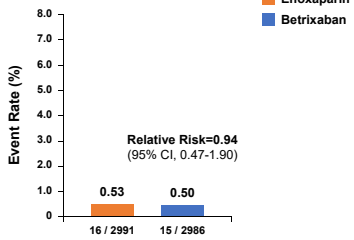
Primary Efficacy and Safety Endpoint (cont)

80-mg dose

PRIMARY EFFICACY OUTCOME
Total VTE or VTE-Related Death
mITT Population



PRIMARY SAFETY OUTCOME
Major Bleeding
Safety Population



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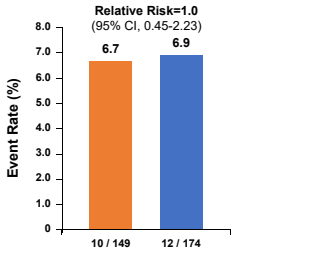
Primary Efficacy Endpoint

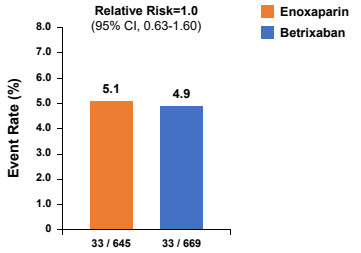
40-mg dose

Total VTE or VTE-Related Death
mITT Population

Severe Renal Impairment
(CrCl 15-30 mL/min)



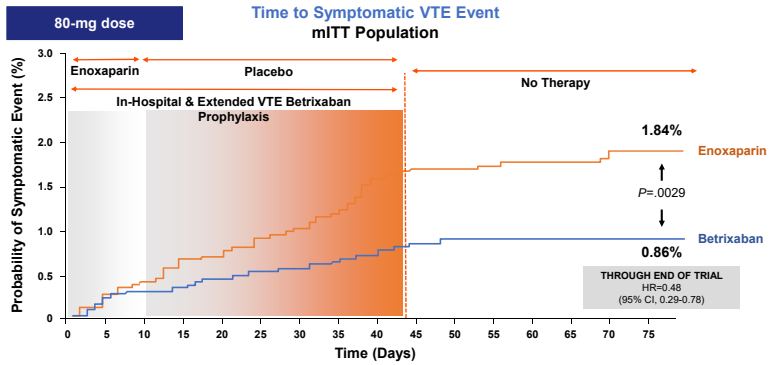
Concomitant P-gp Inhibitor Use



FDA [website]. Drugs@FDA approved drug products. https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&applno=208383. Accessed February 1, 2018. Cohen AT, et al. *N Engl J Med*. 2016;375(6):534-544.

Time to Symptomatic VTE Event Through End of Trial (Post Hoc)

80-mg dose

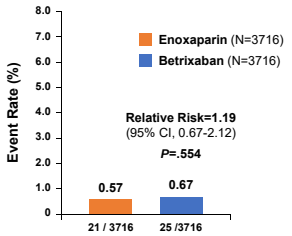


Gibson CM, et al. Modified poster presented at ISTH SSC 2016; May 25-28, 2016; Montpellier, France.

Primary Safety Endpoint

80-mg & 40-mg doses

PRIMARY SAFETY OUTCOME
Major Bleeding
Safety Population



PRIMARY SAFETY OUTCOME
Types of Major Bleeding
Safety Population

	Enoxaparin (N=3716) n (%)	Betrixaban (N=3716) n (%)
Gastrointestinal	9 (0.24)	19 (0.51)
Intracranial hemorrhage	7 (0.19)	2 (0.05)
Intraocular	1 (0.03)	0 (0)
Fatal bleeding	1 (0.03)	1 (0.03)

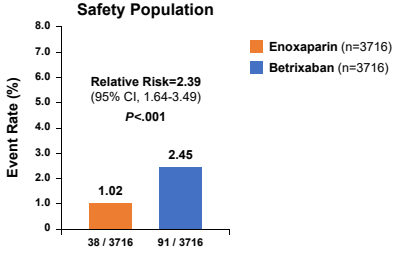
FDA [website]. Drugs@FDA approved drug products. https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&applno=208383. Accessed February 1, 2018. Cohen AT, et al. *N Engl J Med.* 2016;375(6):534-544.

Secondary Safety Endpoint: CRNM Bleeding

80-mg & 40-mg doses

- Most CRNM bleeding events were mild to moderate in severity and did not require or prolong hospitalization
  - CRNM is defined as overt bleeding not meeting criteria for major bleeding but associated with medical intervention, unscheduled contact with a physician, cessation of study treatment, or with discomfort for the patient

CRNM Bleeding
Safety Population



CRNM = clinically relevant non-major.
FDA [website]. Drugs@FDA approved drug products. https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&applno=208383. Accessed February 1, 2018.

Risk Stratification Tools, Patient-Specific Factors, and Shared Decision-Making

- **Objective 4:** Incorporate risk stratification tools, patient-specific factors, and shared decision-making within the identification of patients who would most benefit from extended VTE prophylaxis
- **Risk Stratification Tools and Patient-Specific Factors**
  - Padua Prediction Score for Risk of VTE (https://www.mdcalc.com/padua-prediction-score-risk-vte)
  - International Medical Prevention Registry on Venous Thromboembolism (IMPROVE VTE Risk Assessment; http://www.outcomes-umassmed.org/improve/risk_score/index.html)
- **Shared Decision-Making/Team-Based Care**
  - An Interdisciplinary Approach to Preventing VTE (https://scholarsphere.psu.edu/downloads/6t148fg135)

Patient Case: 76-Year-Old Man with Heart Failure[a]

[a]This is a hypothetical patient case.

Patient Case: 76-Year-Old Man with Heart Failure (cont)

Initial presentation

- A 76-year-old man is admitted to the ED with persistent cough, dyspnea, and bilateral edema in the legs and is diagnosed with an acute heart failure exacerbation
- He has difficulty moving about and was brought to the ED by his wife, who says that because of his breathing difficulty, he was experiencing restricted mobility and was unable to get out of bed for the past 3 days, unless absolutely necessary

Medical history

- CHF (NYHA class III), LVEF 29%
- Hypertension
- BPH
- GERD

Current medications

- Lisinopril
- Furosemide
- Tamsulosin
- Esomeprazole

Allergies

- Penicillin

Social history

- Retired teacher who lives with his wife, who is his primary caretaker

ED = emergency department; CHF = congestive heart failure; LVEF = left ventricular ejection fraction; BPH = benign prostatic hyperplasia; GERD = gastroesophageal reflux disease.

Patient Case: 76-Year-Old Man with Heart Failure (cont)

Height	Weight	BMI
5'7"	72.5 kg	25.1 kg/m^2

Pertinent physical examination findings

- **Neck:** Jugular venous distension
- **Chest:** Lungs are dull to percussion with bilateral crackles; x-ray shows bilateral pleural effusions and cardiomegaly
- **Heart:** S3 gallop noted, RRR, no fibrillation or flutter
- **Extremities:** Bilateral lower extremity edema, minimal clubbing
- **Abdomen:** Liver edge palpable and tender, consistent with hepatomegaly

Vitals

- **HR:** 112 bpm
- **BP:** 150/90 mm Hg
- **RR:** 24
- **Temp:** 99° F
- **O_2 saturation:** 91%

BMP

Na 133	Cl 93	BUN 33	Glu 112
K 3.9	HCO_3 23	Cr 1.6	

CrCl

40 mL/min (Cockroft-Gault using actual body weight)

CBC

- **WBC:** 6300 cells/mcL (normal differential)
- **Hgb/Hct:** 15.6 g/dL /44%
- **Platelets:** 230,000/m^3

Urinalysis

Normal

LFTs

Normal

Other

Normal PT and INR

BMI = body mass index; BMP = basic metabolic panel; BP = blood pressure; bpm = beats per minute; BUN = blood urea nitrogen; CBC = complete blood count; Hgb = hemoglobin; Hct = hematocrit; HR = heart rate; INR = international normalized ratio; LFT = liver function test; PT = prothrombin time; RR = respiratory rate; RRR = regular rate and rhythm; Temp = temperature; WBC = white blood cells.

Patient Case: 76-Year-Old Man with Heart Failure (cont)

Assessment of VTE risk

Risk factors for VTE in this patient include:
- Limited mobility (bedridden for 3 days and anticipated length of hospitalization at least 4 days)
- Hospitalization for heart failure (candidate for admission)
- 76 years old

APEX criteria met

- Aged ≥40 years
- Hospitalization for acute medical illness (heart failure)
- Moderate to severe immobilization at least 24 hours and expected hospitalization at least 3 days

PADUA prediction score

Risk Factor	Points
Heart failure	1
Elderly (≥70 years)	1
Immobilization for ≥3 days	3
Total score Scores ≥4 associated with high VTE risk	**5**

Improve VTE risk assessment

Risk Factor	Points
Aged >60 years	1
Immobilization for at least 7 days (prior to and during hospital admission)	1
Total score Scores ≥2 associated with high VTE risk	**2**

Patient Case: 76-Year-Old Man with Heart Failure (cont)

Patient management Audience Response Question

- Patient requires observation in the ED for 48 hours for decompensated CHF, later transferred to the general medical floor, and hospitalized for a total of 7 days
- During his hospitalization, the patient receives supplemental oxygen to manage hypoxemia and IV diuretics for volume overload
- He is a candidate for extended VTE prophylaxis
- QUESTION: Which of the following medications should he receive?
  - A. Enoxaparin
  - B. Apixaban
  - C. Betrixiban
  - D. Rivaroxaban

IV = intravenous.

Coordinated Transitions of Care

- **Objective 5:** Lead the interdisciplinary care team in the management of anticoagulant therapy for VTE prophylaxis, ensuring individualized therapeutic selection, patient-centric education and monitoring, and coordinated transitions of care from hospital to outpatient settings
- **Transitions of Care**
  Successful transitions of care require:
  1. Complete and accurate exchange of information
  2. Care management, medication continuity, laboratory monitoring
  3. Communication between healthcare professionals and the patient and caregivers (often the weak link)
  4. Pharmacists can play a central role in transitions of care
     - Jackson Memorial Hospital (Miami) DVT Program
     - Patient Education, Treatment, and Patient Selection
     - Reduced LOS, ED Visit Time Reduced

Owens GM, et al. *Am J Manag Care.* 2014;20:S81-S91. Lenchus JD. *Adv Ther.* 2016;33:29-45.

Summary

- In medically ill patients, **60% of VTE risk accumulates from admission to 40 days**
- Betrixaban is the **only current oral anticoagulant indicated** for prophylaxis of VTE in adult patients hospitalized for an acute medical illness who are at risk for thromboembolic complications due to moderate or severe restricted mobility and other VTE risk factors
- Betrixaban 80 mg demonstrated a **32% relative risk reduction** in VTE and VTE-related death vs enoxaparin (NNT=50)
- Will all DOACs use caution in conditions where an **increased risk of bleeding** exists or is suspected?
  - All DOACs increase the risk of bleeding and can cause serious and potentially fatal bleeding
  - Caution may occur in patients undergoing neuroaxial anesthesia or spinal puncture–long-term permanent paralysis
  - Caution with drugs affecting hemostasis: Aspirin, antiplatelet drugs, other anticoagulants, heparin, selective serotonin reuptake inhibitors, and nonsteroidal anti-inflammatory drugs
  - We remain without an active reversal agent for factor X DOACs

Questions?

Additional Slides for Q/A Only

Phase 3: Acknowledge Risk of Emotional Harm

- **Updated 'welcome letter' and external webpage**
  - *"…people who have a blood clot can feel anxious or depressed. If you or a family member are worried about your behavior or feelings, please let us know, so we can offer help."*
  - Online resources/patient support groups added
- **Reference card with open-ended questions (target first 30 days post-VTE)**
  - What questions do you have about our educational materials or online resources?
  - What concerns have you had about bleeding?
  - What concerns have you had about having another clot?
  - How has your recent clot affected you emotionally?

Document positive findings

Phase 3: Responding to Emotional Harm

- **How should you respond to patients who are experiencing emotional harms?**
  - *"These feelings are not uncommon, and we do have resources available to help. Would you like me to explain the resources we have that could help?"*
  - PULSE – "Patient Resources" page

Emotional Distress Support

1. May refer to PCP or Thrombosis MD
2. Offer Online Support Groups
   a. North American Thrombosis Forum
   b. National Blood Clot Alliance
3. Refer to Social Workers in Community Clinics
4. Crisis Intervention & Hospital Diversion Services

Document if any of these are offered