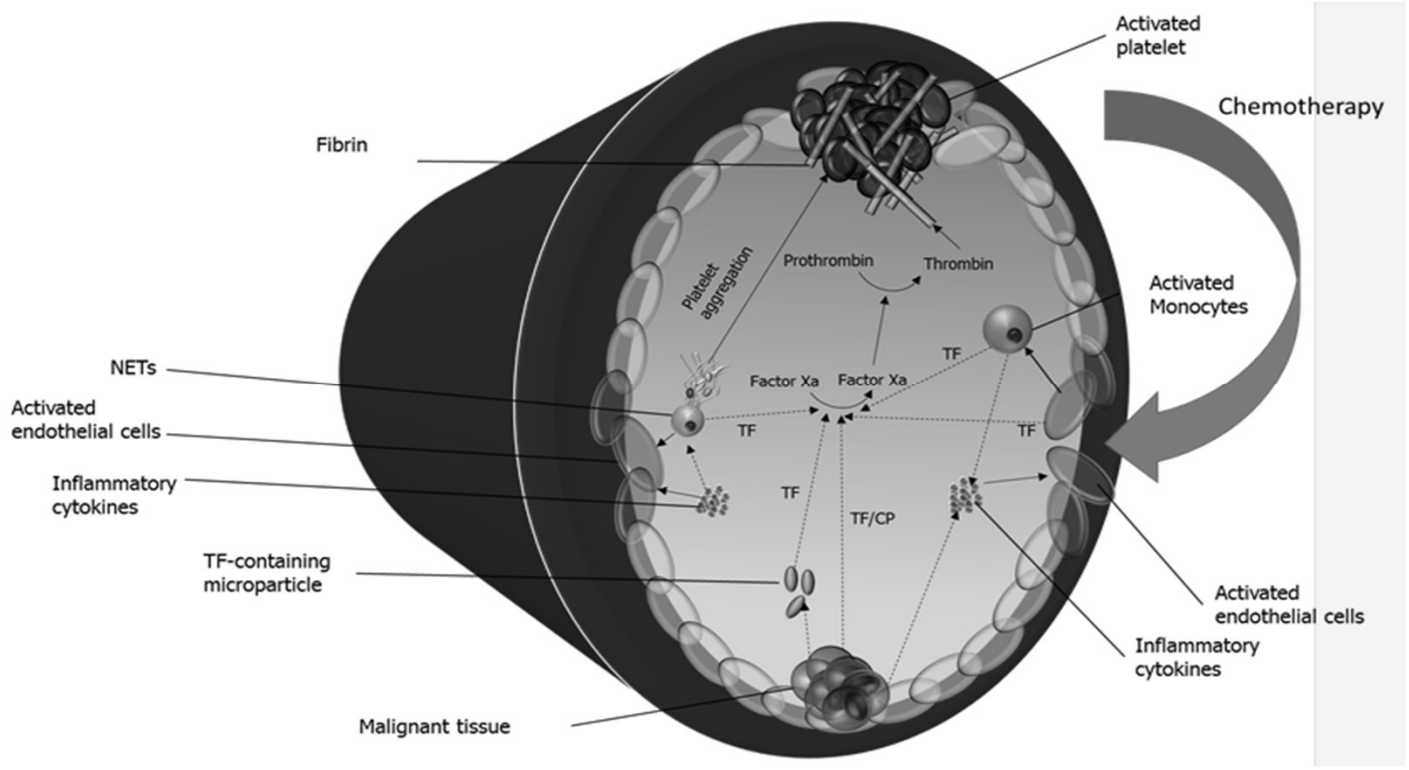
ĐIỀU TRỊ VTE Ở BỆNH NHÂN ĐANG CÓ UNG THƯ: HEPARIN CÓ PHẢI LÀ LỰA CHỌN DUY NHẤT?

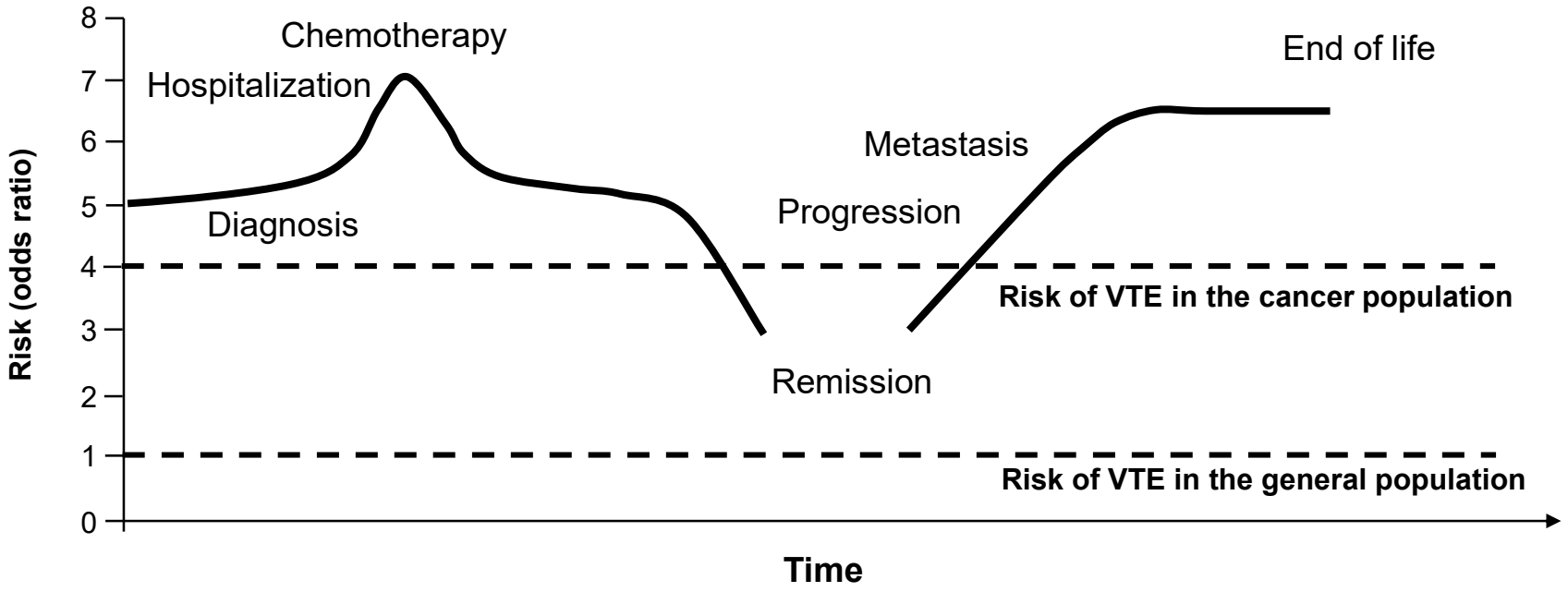
GS TS BS VÕ THÀNH NHÂN
ĐH Y Dược – BV Vinmec Central Park – Liên Chi Hội Tim Mạch Can Thiệp
TP Hồ Chí Minh

Ung thư có liên quan đến tình trạng tăng đông máu: Các con đường được đề xuất trong sinh bệnh học CAT



Ay C *et al*, *Thromb Haemost* 2017;117:219–230

Nguy cơ VTE thay đổi theo diễn tiến tự nhiên của bệnh ung thư[1,2]



Overall, incidence rate of VTE is:
5.8 (95 % CI 5.7–6.0) per 100 patient-years[3]

1. Lyman GH, *Cancer* 2011;117:1334–1349; 2. Rao MV *et al*, Who's at risk for thrombosis? In: *Cancer-associated thrombosis: new findings in translational science, prevention, and treatment*. New York: Informa Healthcare; 2007:1691–1692; 3. Cohen AT *et al, Thromb Haemost* 2017;117:57–65

Huyết khối do ung thư (CAT) làm giảm tiên lượng sống

CAT is related to a 30-fold increased risk of death

Exposure	Patien	Mortality per 100	HR (95% CI)
None			e)
VTE only			3)
Cancer only			2)
Cancer and VTE			9.6)

"You don't die of a tumor right away but do of a pulmonary embolism."

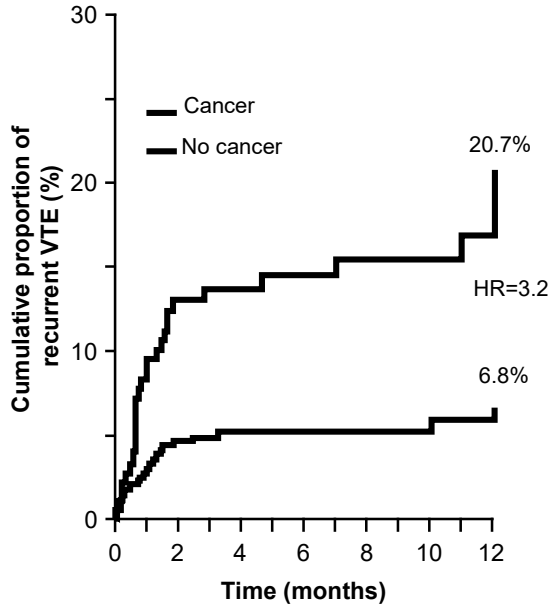
Adapted from Market Understanding - VTE among Oncologists - Produkt + Markt Healthcare - November 2017 - Full Report - L.DE.MR.GM.09.2017.4218

Timp JF *et al*, *Blood* 2013;122:1712–1723

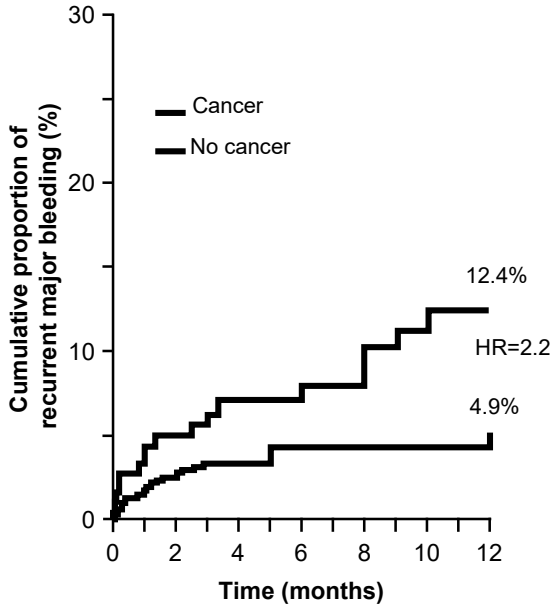
Thách thức khi điều trị kháng đông cho bệnh nhân VTE có ung thư

Ung thư làm gia tăng nguy cơ tái phát VTE cũng như nguy cơ chảy máu nặng khi dùng kháng đông.

Tái phát VTE



Chảy máu nặng*



*Defined as overt and associated with either a decrease in the haemoglobin level (at least 2.0 g/dl) or the need for transfusion (≥2 units of blood), if it was retroperitoneal or intracranial, or if the treatment had to be discontinued permanently

Prandoni P *et al*, *Blood* 2002;100:3484–3488

Tiếp cận điều trị và dự phòng cho BN ung thư có VTE như thế nào?

ACCP 2016 Guidelines: Acute Treatment and Secondary Prevention of VTE

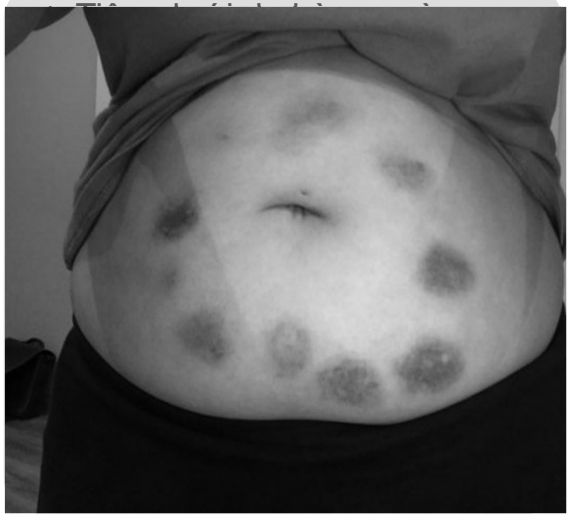
	ACCP recommendation	Grade of recommendation
Initial anticoagulation		
Acute DVT or haemodynamically stable PE and no cancer	NOAC preferred to LMWH/VKA	2B
	LMWH/VKA preferred to LMWH alone	2C
PE with hypotension	Thrombolytic therapy (systemic rather than catheter-directed unless bleeding risk is high)	2B (2C)
DVT or PE with cancer	LMWH suggested over NOAC or VKA	2C
Duration of anticoagulant therapy		
Proximal DVT or PE	3 months recommended over shorter duration	1B
First proximal DVT or PE provoked by surgery or other transient risk factor	3 months	1B (2B if low/moderate bleeding risk; 1B if high)
Unprovoked DVT or PE	Extended therapy if bleeding risk is low/moderate	2B
	3 months if bleeding risk is high	1B
DVT or PE associated with active cancer	Extended therapy recommended over 3 months' therapy	1B (2B if high bleeding risk)

Kearon C *et al*, *Chest* 2016;149:315–352

Cân nhắc khi lựa chọn kháng đông trên BN CAT

VKAs[1–4]

LMWHs



NOACs[5–8]

- Liều [illegible] và không cần

Bên cạnh tính thuận tiện, liệu NOAC có hiệu quả và an toàn trên BN ung thư có VTE?

loại khối u, ví dụ: ung thư đường tiêu hóa

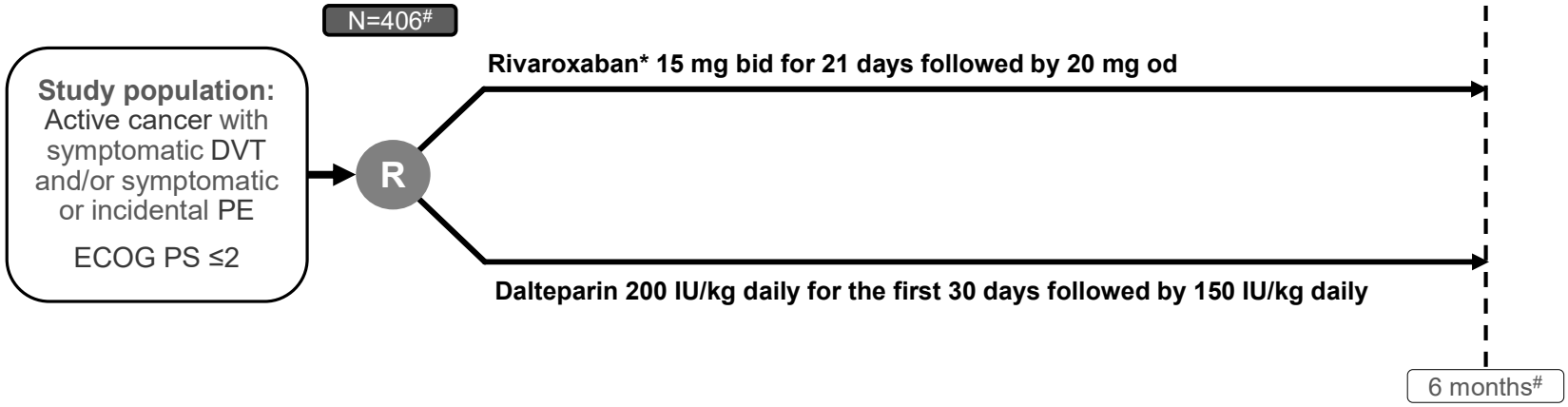
Các đặc điểm thuận lợi của kháng đông có ý nghĩa trên BN ung thư vốn thường phải sử dụng cùng lúc nhiều thuốc và các điều trị hỗ trợ

1. Prins M *et al*, *Lancet Haematol* 2014;1:e37–e46; 2. Lee AYY *et al*, *N Engl J Med* 2003;349:146–153; 3. Lee AYY *et al*, *JAMA* 2015:341:677–686;
4. Alk EA *et al*, *Cochrane Database Rev* 2014;7:CD006650; 5. Cohen ATC *et al*, *Thromb J* 2018;16:21; 6. Young A *et al*, *J Clin Oncol* 2018;36:2017–2023;
7. Raskob GE *et al*, *N Engl J Med* 2018;378:615–624; 8. Riva N *et al*, *Blood Transfus* 2015;13:181–183

Bên cạnh tính thuận tiện, liệu NOAC có hiệu quả và an toàn trên BN ung thư có VTE?

SELECT-D: Nghiên cứu pha III Rivaroxaban vs Dalteparin[1,2]

Study design: Prospective, randomized, open-label, multicentre pilot study



*A dose reduction or discontinuation was specified for different levels of renal impairment; #the second randomization phase for extended treatment of VTE from 6 to 12 months for patients with PE as an index event or patients with residual DVT at 5-month assessment was closed due to low recruitment. Required sample size reduced from 530 to 400 patients for main trial comparison (95% CI for VTE recurrence ± 4.5%)

1. Young A *et al*, *Thromb Res* 2016;140:S172–S173; 2. Young A *et al*, *J Clin Oncol* 2018;36:2017–2023

Select-D: Outcomes, Inclusion and Exclusion Criteria

Primary outcome

- To assess **VTE recurrence rates*** (including symptomatic VTE and incidental PE)

Key secondary outcomes

- **Major bleeding** and clinically relevant non-major bleeding#
- Feasibility to evaluate extended anticoagulation treatment beyond 6 months in selected patients
- Acceptability and **compliance**
- **Treatment satisfaction** (ACTS)
- **QoL** (EuroQol [EQ-5D-5L] and SF36® health survey questionnaire)

Key inclusion criteria

- Active cancer
- Objectively confirmed VTE (symptomatic lower extremity proximal DVT or symptomatic/incidental PE)
- ECOG performance status score ≤2
- Adequate haematological function‡
- Adequate renal and hepatic function§

Key exclusion criteria

- >72 hours' pretreatment with anticoagulant prior to randomization¶
- Previous history of VTE
- Requirement for antiplatelet therapy**
- Bacterial endocarditis
- SBP >180 mmHg or DBP >110 mmHg##
- Bodyweight <40 kg at time of VTE
- Contraindications according to EU label

*Investigator-reported recurrent VTE; #all bleeding outcomes were independently adjudicated; ‡recommended levels: haemoglobin >100 g/l, white cell count >2×10^9/l, platelets >100×10^9/l; §liver enzymes <3 × ULN; CrCl ≥30 ml/min; ¶this can be extended to 96 hours if required; **other than ASA ≤75 mg daily; ##control of blood pressure using anti-hypertensive drugs is permitted

Young A *et al*, *Thromb Res* 2016;140:S172–S173; EudraCT number: 2012-005589-37; Bach M *et al*, *Thromb Haemost* 2016;116:S24–S32

Select-D: Patients Baseline Characteristics

Baseline characteristics

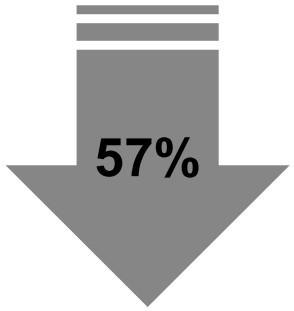
	Rivaroxaban (n=203)	Dalteparin (n=203)
Age, years, median (range)	67 (22–87)	67 (34–87)
Gender male, %	54	48
Metastatic cancer, %	59	59
ECOG performance status, % 0 or 1 2	 72 26	 76 21
Qualifying VTE, % Symptomatic VTE Incidental PE	 46 54	 48 52

Primary tumour type

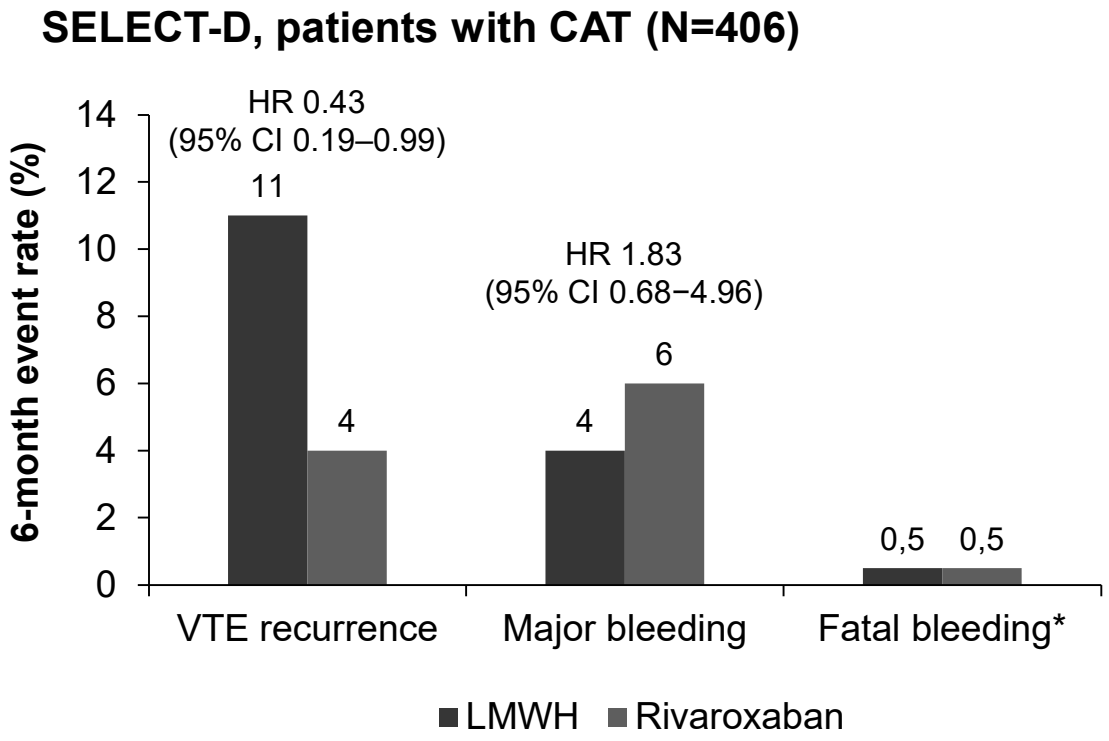
Tumour type, %	Rivaroxaban (n=203)	Dalteparin (n=203)
Colorectal	27	23
Lung	11	12
Breast	9	10
Ovarian	5	9
Pancreatic	9	5
Lymphoma	5	6
Oesophageal/ gastro-oesophageal	5	9
Prostate	6	3
Bladder	5	2
Other	18	21

Young A *et al*, ASH 2017: Abstract 625; Available at: http://www.clinicaltrialresults.org/

Rivaroxaban dự phòng hiệu quả tái phát VTE mà không tăng nguy cơ xuất huyết



Decrease in VTE recurrence

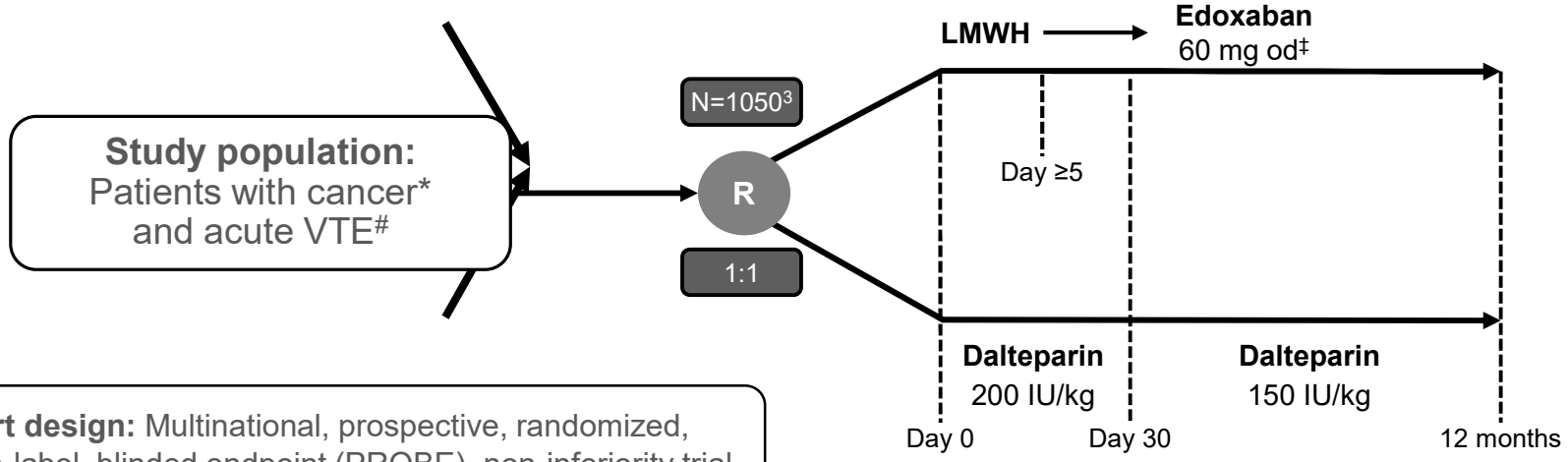


*One fatal bleeding event in each arm.

Young A et al. *J Clin Oncol* 2018;36:2017–2023.

Hokusai-VTE-Cancer: Edoxaban[1–3]

Mục tiêu: đánh giá hiệu quả và an toàn của edoxaban (sau ≥5 ngày dùng LMWH) so với dalteparin trong điều trị VTE trên BN ung thư*

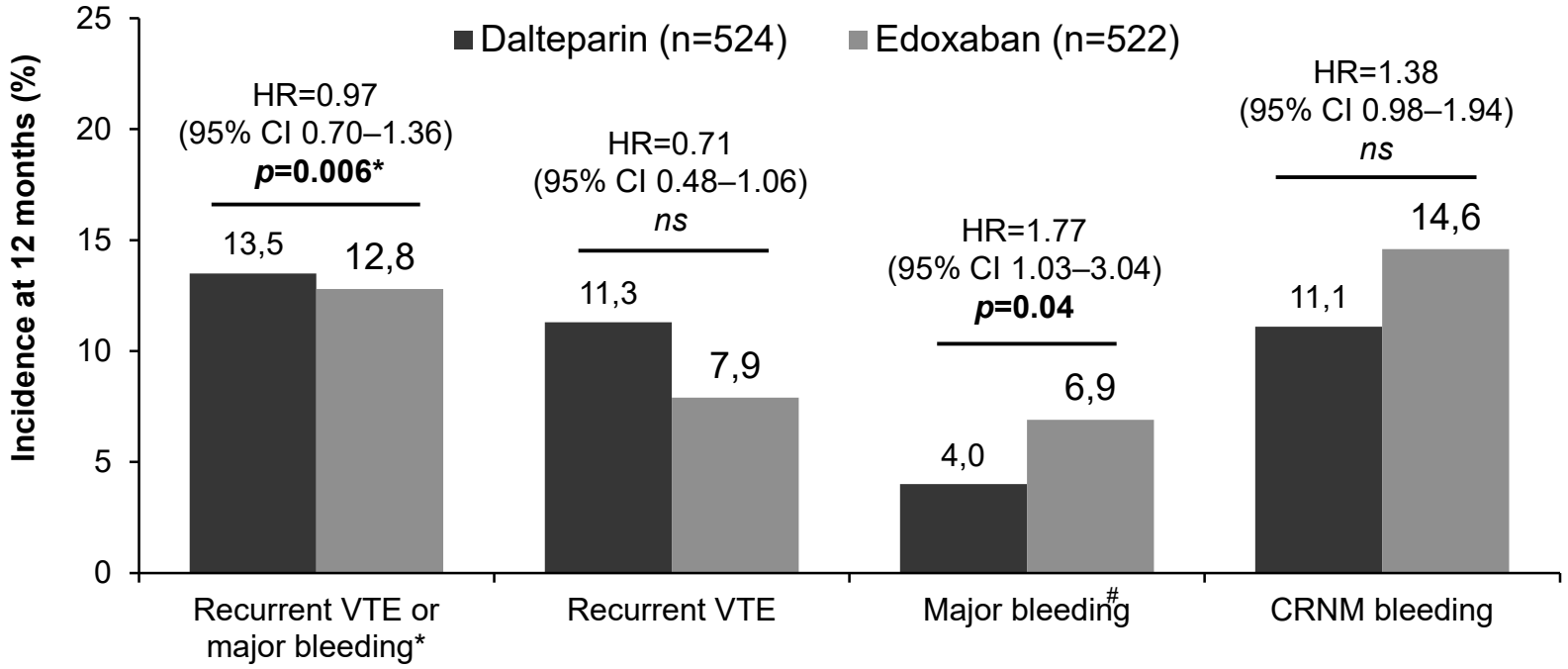


Short design: Multinational, prospective, randomized, open-label, blinded endpoint (PROBE), non-inferiority trial

*Cancer must be other than basal-cell or squamous cell carcinoma of the skin, be active or diagnosed within 2 years prior to randomization and objectively confirmed. Active cancer was defined as any of the following: diagnosis of cancer within the past 6 months; recurrent, regionally advanced or metastatic disease; currently receiving treatment or having received any treatment for cancer during the 6 months prior to randomization; or a haematological malignancy not in complete remission; #incidental proximal lower extremity DVT or symptomatic or incidental PE or both; ‡dose adjustment to 30 mg od in patients with a body weight ≤60 kg or CrCl 30–50 ml/min, or concomitant use of P-glycoprotein inhibitors

1. Daiichi Sankyo, Inc. https://clinicaltrials.gov/ct2/show/NCT02073682 [accessed 09 Dec 2019]; 2. van Es *et al*, *Thromb Haemostat* 2015;114;1268–1276; 3. Raskob *et al, N Engl J Med* 2018;378:615–624

Hokusai-VTE-Cancer: So với Dalteparin, BN dùng edoxaban có tỷ lệ tái phát thấp hơn nhưng xuất huyết nặng cao hơn

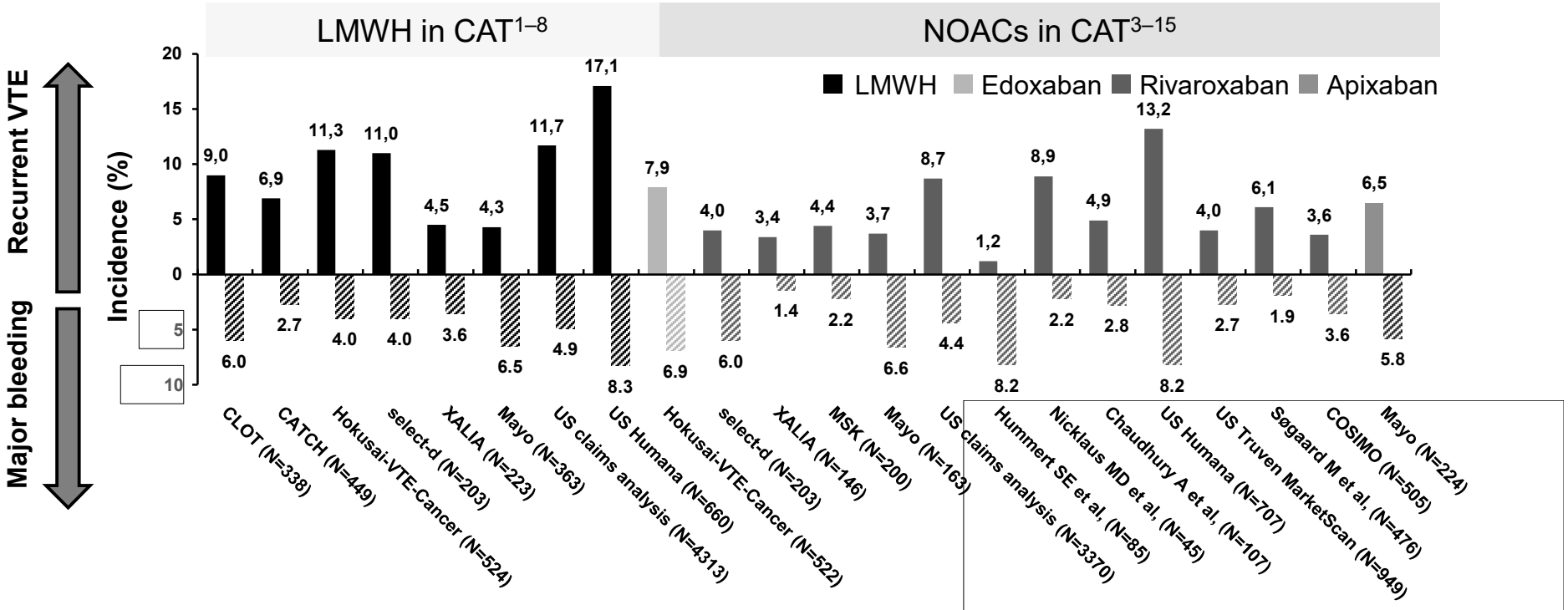


*Primary outcome with *p*-value for non-inferiority; #there was one fatal bleeding event in the dalteparin arm, 0 in the edoxaban arm

Raskob GE *et al*, *N Engl J Med* 2018;378:615–624

Dữ liệu sử dụng NOAC điều trị CAT trong thực tế lâm sàng

Tổng hợp các nghiên cứu của kháng đông trên BN CAT



Results reported during ~6 months follow-up period with the expectation of the Hokusai-VTE-Cancer study and the XALIA study which had 12 month observation periods

Data should be interpreted with caution due to different types of studies. No cross study comparison intended

1. Lee AYY *et al*, *N Engl J Med* 2003;349:146–153; 2. Lee AYY *et al*, *JAMA* 2015;314:677–686; 3. Raskob *et al, N Engl J Med* 2018;378:615–624; 4. Young A *et al*, *J Clin Oncol* 2018;36:2017–2023; 5. Ageno W *et al*, *TH Open* 2017;1:e33–e42; 6. Wysokinski WE *et al, Am J Hematol* 2019;94:1185–1192; 7. Khorana AA *et al*, ASH 2017: Abstract 4631; 8. Streiff MB *et al*, *Am J Hematol* 2018;93:664–671; 9. Mantha S *et al*, *J Thromb Thrombolysis* 2017;43:166–171; 10. Hummert SE *et al*, ASCO 2017: Abstract e18268; 11. Nicklaus MD *et al*, *J Oncol Pharm Pract* 2017;24:185–189; 12. Chaudhury A *et al*, *Indian J Hematol Blood Transfus* 2017;34:530–534; 13. Kohn CG *et al*, *Natl Compr Canc Netw* 2018;16:491–497; 14. Søgaard M *et al*, *Cancer Med* 2019;8:1044–1053; 15. Maraveyas A *et al,* ASH. 2019, Poster 2161

RWE 1

Received: 3 October 2017 | Revised: 22 January 2018 | Accepted: 31 January 2018
DOI: 10.1002/ajh.25059

RESEARCH ARTICLE

WILEY AJH

Effectiveness and safety of anticoagulants for the treatment of venous thromboembolism in patients with cancer

- Humana database: January 2007 to June 2015
- Total 2428 newly diagnosed cancer patients: 1061 treated with warfarin, 707 with rivaroxaban, and 660 with LMWH.
- Median duration of therapy with LMWH (1.0 month) was shorter than for rivaroxaban (3.0 months) and warfarin (3.5 months)

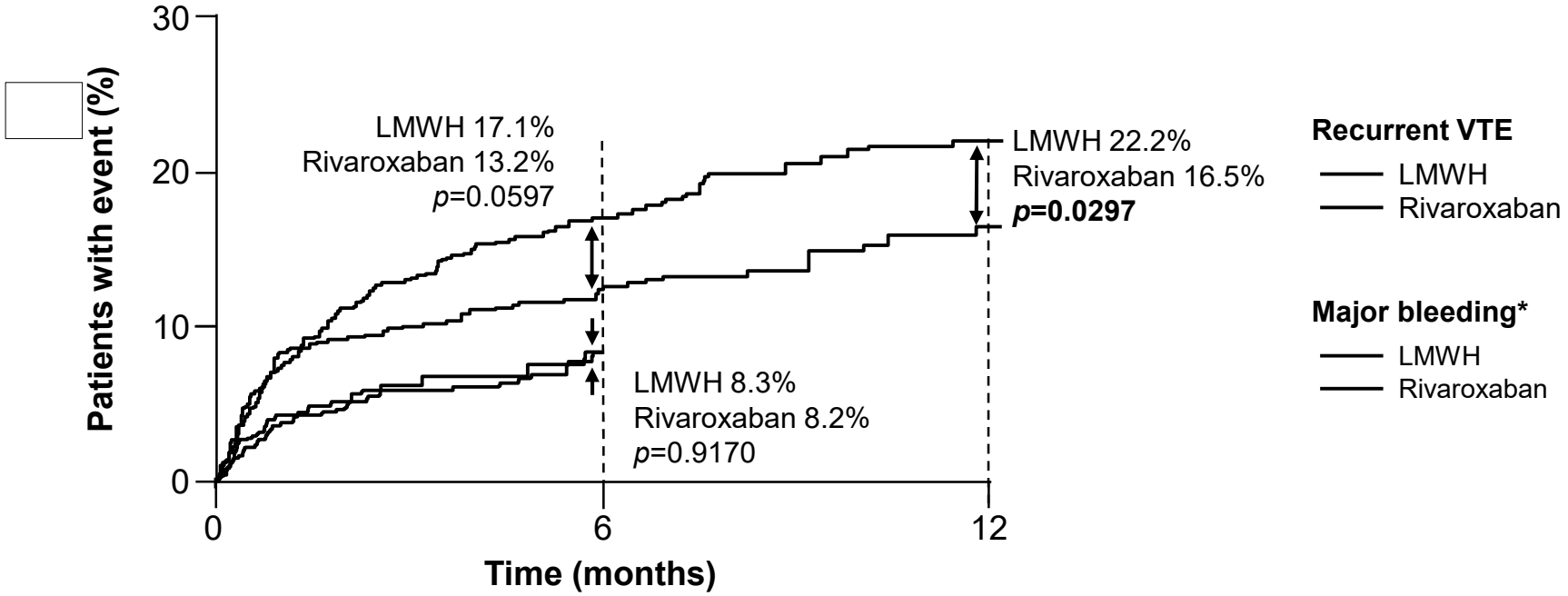
*Data to 6 months only. Humana Database from January 2007 to June 2015; N=2428 newly diagnosed cancer patients with VTE (rivaroxaban n=707; LMWH n=660).

Streiff MB et al. *Am J Hematol* 2018;93:664–671.

RWE: Real-World Evidence

RWE 1

Dữ liệu thực tế lâm sàng cho thấy hiệu quả và an toàn của rivaroxaban



*Data to 6 months only. Humana Database from January 2007 to June 2015; N=2428 newly diagnosed cancer patients with VTE (rivaroxaban n=707; LMWH n=660).

Streiff MB et al. *Am J Hematol* 2018;93:664–671.

RWE 1

Trung bình, khi thay thế LMWH bằng rivaroxaban, cứ 18 BN sẽ có thêm 1 BN được bảo vệ khỏi tái phát VTE

Number needed to treat (NNT) to prevent one event

NNT= 18

versus LMWH
over 1 year

Streiff MB et al. *Am J Hematol* 2018;93:664–671.

ARR=(Controleventrate)−(Experimentaleventrate)ARR=0.222−0.165=0.057
NNT=1/ARR=1/0.057=17.5

RWE 2

Mayo Thrombophilia Clinic: Rivaroxaban, Apixaban or LMWH for the Treatment of CAT

Phương pháp

- BN CAT* cấp được chọn từ 01/3/2013 đến 30/01/2018
- BN dùng rivaroxaban, apixaban hay LMWH# trong vòng 14 ngày đầu tiên sau khi được chẩn đoán, và hoàn tất ≥3 tháng dùng kháng đông

Cancer characteristics at baseline‡

Scenario, n (%)	Rivaroxaban (n=163)	Apixaban (n=224)	LMWH (n=363)
Chemotherapy	103 (64.0)	151 (68.0)	246 (68.9)
Metastatic	86 (56.2)	119 (58.3)	209 (64.9)
Ottawa score			
Mean ± SD	−0.4±1.20	−0.4±1.20	−0.6±1.15
Median (range)	0.0 (−2.0, 2.0)	0.0 (−2.0, 3.0)	−1.0 (−2.0, 2.0)

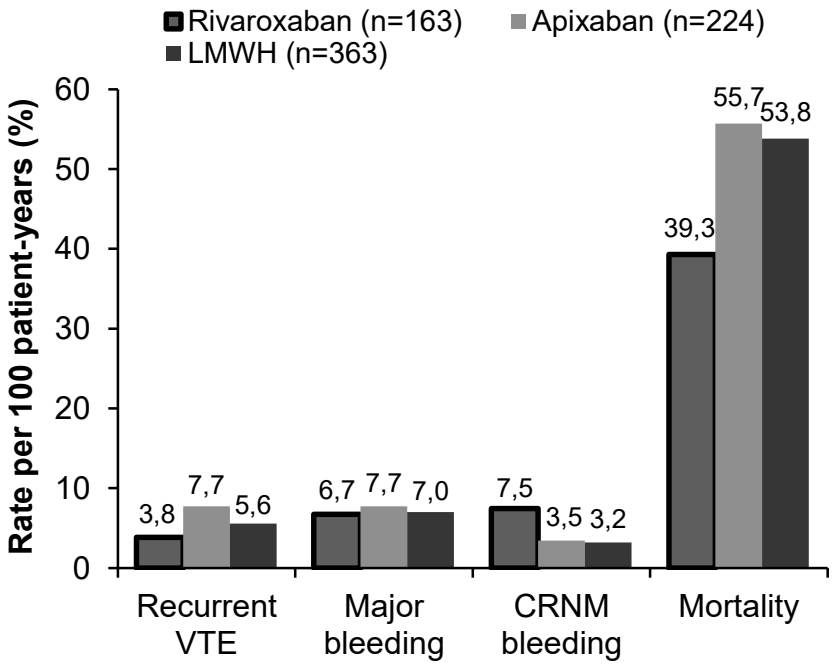
*Active cancer was defined as any evidence of cancer on computerized tomography or positron emission tomography imaging, cancer-related surgery, chemotherapy or radiation therapy within the past 6 months or haematological cancer that was not in complete remission; #anticoagulant selection based on patient characteristics (ability to take medication once or twice a day, renal function); ‡no significant differences between treatment arms

Wysokinski WE *et al*, *Am J Hematol* 2019;94:1185–1192

RWE 2

Mayo Thrombophilia Clinic: Rivaroxaban, Apixaban or LMWH for the Treatment of CAT

Rivaroxaban giảm tỷ lệ tử vong nhiều hơn LMWH và apixaban



	Apixaban vs rivaroxaban	Rivaroxaban vs LMWH
	HR (95% CI); *p*-value	
Recurrent VTE	1.31 (0.51–3.36); 0.57	0.85 (0.36–2.06); 0.73
Major bleeding	0.73 (0.32–1.66); 0.45	1.23 (0.61–2.50); 0.57
CRNM bleeding	0.31 (0.11–0.91); 0.03	2.84 (1.24–6.50); 0.01
Mortality	1.67 (1.20–2.33); 0.002	0.73 (0.56–0.96); 0.03

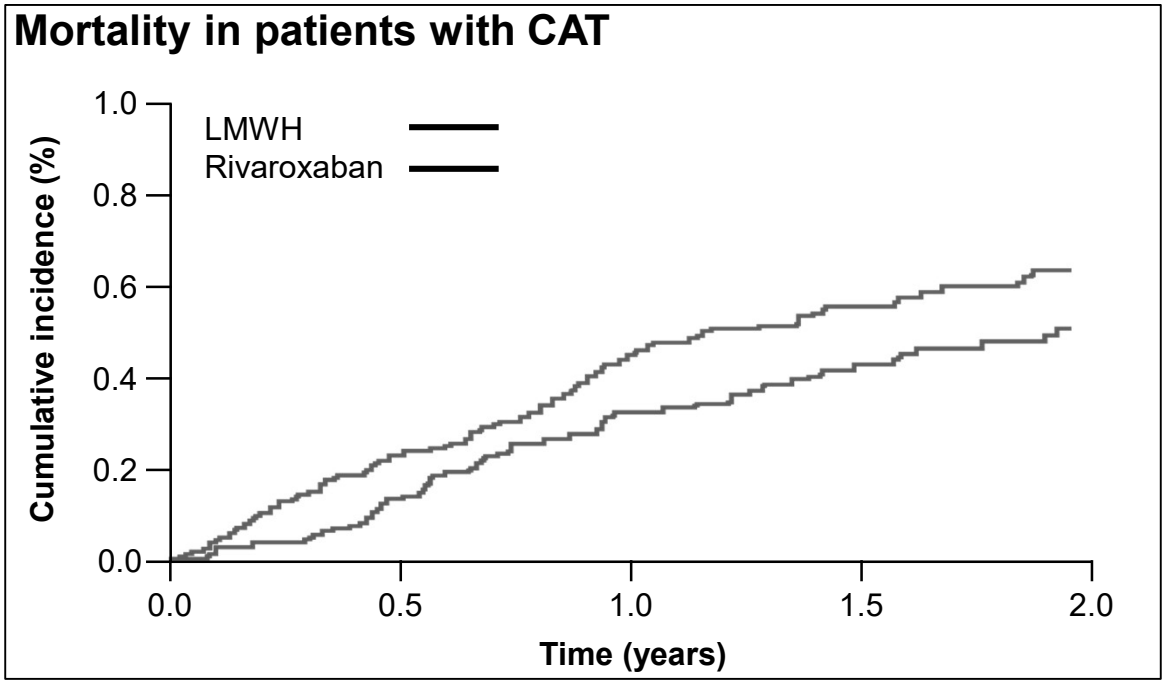
The most common sites of bleeding were the gastrointestinal and genitourinary tract. Three patients treated with apixaban and two with enoxaparin died because of intracranial bleeding to the tumour. There were no known deaths from VTE recurrence

Wysokinski WE *et al*, *Am J Hematol* 2019;94:1185–1192

CRNM: clinical relevant non major bleeding

RWE 2

Rivaroxaban giảm tỷ lệ tử vong nhiều hơn so với LMWH



Rivaroxaban	163	70	30
LMWH	363	94	34

27%

Lower mortality compared with LMWH

HR 0.73
(95% CI 0.56–0.96)

VTE recurrence and major bleeding were similar in both arms

Wysokinski WE et al. *Am J Hematol* 2019;94:1185–1192.

Cập nhật các guidelines mới nhất về điều trị CAT

Cập nhật các khuyến cáo mới nhất về điều trị CAT

	ISTH SSC 2018[1]	ASCO 2019[2]	ITAC 2019[3]	NCCN 2019[4]	ESC 2019[5]
Lựa chọn kháng đông	NOACs (edoxaban và **rivaroxaban**) và LMWH là các thuốc được lựa chọn Lựa chọn phụ thuộc vào nguy cơ xuất huyết (LMWH được ưu tiên trên các BN có nguy cơ xuất huyết cao) và khả năng có tương tác giữa các thuốc sử dụng	**Khởi đầu** kháng đông (5-10 ngày đầu tiên): LMWH hay **rivaroxaban** **Dài hạn** (<6 tháng): LMWH, edoxaban hay **rivaroxaban** (VKAs có thể dùng thay thế cho điều trị dài hạn nếu LMWH/NOACs không có sẵn) Điều trị **mở rộng** (≥6 tháng): LMWH, edoxaban hay **rivaroxaban** hay VKAs	**Khởi đầu** kháng đông (5-10 ngày đầu tiên): LMWH, **rivaroxaban** (ngay từ ngày đầu tiên) hay edoxaban sau khi dùng ≥5 ngày kháng đông chích **Dài hạn** (<6 tháng): LMWH hay NOACs (hiện nay, chỉ có bằng chứng cho edoxaban và **rivaroxaban**) Điều trị **mở rộng** (≥6 tháng): LMWH hay NOACs	Liệt kê các đơn trị liệu hay phối hợp điều trị bao gồm edoxaban, **rivaroxaban** và apixaban	Điều trị dài hạn các BN PE kèm ung thư (<6 tháng): LMWH được ưu tiên hơn VKAs Edoxaban hay **rivaroxaban** nên được cân nhắc thay thế LMWH, nhưng phải thận trọng trên các BN ung thư đường tiêu hóa vì có nguy cơ tăng xuất huyết đường tiêu hóa
Thời gian điều trị	Không có khuyến cáo chính thức	Điều trị mở rộng trên 6 tháng có thể cân nhắc trên các bệnh nhân đang mắc ung thư	LMWH hay NOACs nên dùng ít nhất 6 tháng, sau đó việc ngưng hay tiếp tục dùng thuốc kháng đông nên được đánh giá trên từng bệnh nhân cụ thể	Không có khuyến cáo chính thức	Điều trị mở rộng nên được cân nhắc trong một thời gian không xác định hay đến khi ung thư được chữa khỏi

1. Khorana AA *et al*, *J Thromb Haemost* 2018;16:1891–1894; 2. Key NS *et al*, *J Clin Oncol* 2019; doi:10.1200/JCO.19.01461; 3. Farge D *et al*, *Lancet Oncol* 2019;20:e566–e581;
4. NCCN guidelines v. 1. 2019. https://www.nccn.org/store/login/login.aspx?ReturnURL=https://www.nccn.org/professionals/physician_gls/pdf/vte.pdf [accessed 23 Oct 2019];
5. Konstantinides SV *et al*. *Eur Heart J* 2019:40:3453–3455

2019 ESC Guidelines for the Management of PE: Patients with Active Cancer (1)

- What's changed? The **2014 guidelines** recommended that weight-adjusted subcutaneous **LMWH be considered for the first 3–6 months** in patients with **cancer and PE**[1]
  - NOACs were not listed as antithrombotic therapeutic options for the treatment of PE in patients with cancer

2019 recommendations for the regimen and the duration of anticoagulation after PE in patients with active cancer[2]	Class of recommendation	Level of evidence
For patients with PE and cancer, weight-adjusted subcutaneous LMWH should be considered for the first 6 months over VKAs	IIa	A
Edoxaban should be considered as an alternative to weight-adjusted subcutaneous LMWH in patients without gastrointestinal cancer	IIa	B
Rivaroxaban should be considered **as an alternative to** weight-adjusted subcutaneous **LMWH** in patients without gastrointestinal cancer	IIa	C

The difference in grading of the level of evidence for edoxaban and rivaroxaban was based on the trial design (phase III vs pilot) and size of the respective trial populations

1. Konstantinides SV *et al*, *Eur Heart J* 2014;35:3033–3069; 2. Konstantinides SV *et al*, *Eur Heart J* 2019:40:3453–3455

2019 ESC Guidelines for the Management of PE: Patients with Active Cancer (2)

- What's changed? The 2014 guidelines recommended that extended anticoagulation (beyond the first 3–6 months) be considered for an **indefinite period** or **until the cancer is cured** in patients with PE and cancer (Class IIa, Level **C**)[1]

2019 recommendations for the regimen and the duration of anticoagulation after PE in patients with active cancer[2]	Class of recommendation	Level of evidence
For patients with **PE and cancer**, extended anticoagulation (beyond the first 6 months) should be considered for an **indefinite period or until the cancer is cured**	IIa	**B**
In patients with cancer, **management of incidental PE in the same manner as symptomatic PE** should be considered, if it involves segmental or more proximal branches, multiple subsegmental vessels, or a single subsegmental vessel in association with proven DVT	IIa	B

1. Konstantinides SV *et al*, *Eur Heart J* 2014;35:3033–3069; 2. Konstantinides SV *et al*, *Eur Heart J* 2019:40:3453–3455

2019 ASCO Guidelines Update for the Treatment of VTE in Patients with Cancer

Initial anticoagulation (5–10 days)	Long-term anticoagulation (<6 months)	Extended anticoagulation (≥6 months)
◆ **Initial anticoagulation may involve LMWH, UFH, fondaparinux or rivaroxaban** ◆ LMWH is preferred over UFH for the initial 5–10 days of anticoagulation for the patient with cancer with newly diagnosed VTE who does not have severe renal impairment (defined as CrCl <30 ml/min)	◆ **LMWH, edoxaban or rivaroxaban for at least 6 months is preferred** because of their improved efficacy over VKAs ◆ VKAs are an acceptable alternative for long-term therapy if LMWH or NOACs are not available	◆ **LMWH, NOACs or VKAs for extended anticoagulation beyond 6 months may be considered for selected patients* with active cancer**

Changes from previous recommendations: rivaroxaban and edoxaban have been added as options for VTE treatment
*Such as those with metastatic disease or receiving chemotherapy

Key NS *et al*, *J Clin Oncol* 2019; doi:10.1200/JCO.19.01461

2019 ITAC Guidelines for the Treatment of VTE in Patients with Cancer

Initial anticoagulation (5–10 days)	Long-term anticoagulation (<6 months)	Extended anticoagulation (≥6 months)
◆ LMWH when CrCl is ≥30 ml/min ◆ **Rivaroxaban** in patients who do not have a high risk of GI or GU bleeding and have a **CrCl ≥30 ml/min** ◆ Edoxaban (following ≥5 days of parenteral anticoagulation) in patients who do not have a high risk of GI or GU bleeding and have a CrCl ≥30 ml/min ◆ (All Grade **1B**)	◆ LMWH is preferred over VKAs when CrCl is ≥30 ml/min (Grade 1A) ◆ **NOACs** are recommended when CrCl is **≥30 ml/min** in the absence of strong DDIs or GI absorption impairment (Grade **1A**)* ◆ Use **caution in** patients with **GI tract malignancies**, especially upper GI tract malignancies	◆ LMWH or NOACs should be used for a **minimum of 6 months** to treat established VTE in patients with cancer (Grade 1A) ◆ **After 6 months**, termination or continuation of anticoagulation (LMWH, NOACs or VKAs) should be **based on individual evaluation** (guidance in the absence of data)

Changes from previous recommendations: previous wording 'NOACs can be considered for VTE treatment of patients with stable cancer not receiving systemic anticancer therapy, and in cases where VKA is an acceptable, but not an available, treatment choice (guidance).'
*Data for other NOACs are needed as it is not clear whether other NOACs will have the same risk profile

Farge D *et al*, *Lancet Oncol* 2019;20:e566–e581

ITAC: The International Initiative on Thrombosis and Cancer

2018 ISTH SSC Guidance on the Use of NOACs for the Treatment of Cancer-Associated VTE

Statement 1

- The use of **NOACs** is suggested for patients with **cancer** and a diagnosis of **acute VTE**, **low risk of bleeding** and no DDIs with current systemic therapy
- Edoxaban and **rivaroxaban** are the only NOACs with current **randomized trial evidence compared with LMWH in patients with cancer**
- LMWH remains an acceptable alternative for these patients

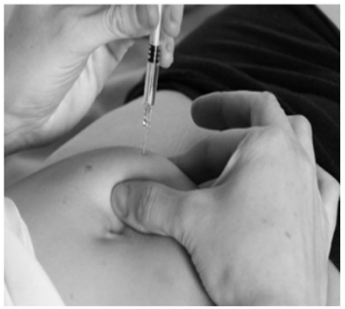
Statement 2

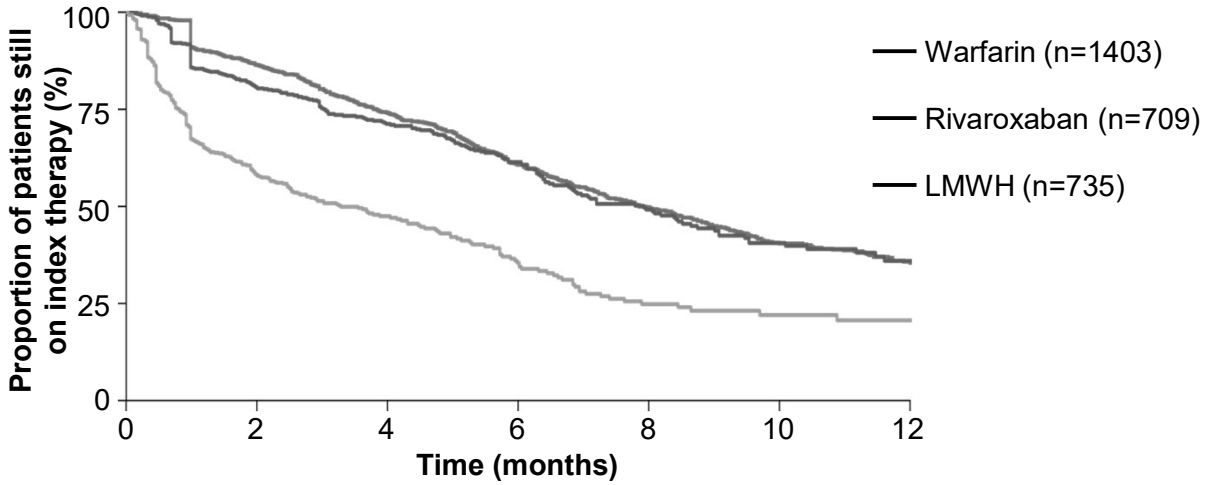
- **LMWH** is suggested for patients with cancer with an acute diagnosis of VTE and **high risk of bleeding**, including: patients with luminal GI cancers with an intact primary, or those with active GI mucosal abnormalities such as duodenal ulcers, gastritis, esophagitis, or colitis
- **NOACs may be an acceptable** alternative if no DDIs exist with current systemic therapy

ISTH SSC, International Society on Thrombosis and Haemostasis Scientific and Standardization Committee

Khorana AA *et al*, *J Thromb Haemost* 2018;16:1891–1894

Thực tế: bệnh nhân điều trị lâu dài hơn với kháng đông đường uống (rivaroxaban và warfarin) so với LMWH





Cohort	Median treatment duration	Kaplan–Meier rates	
		6 months	12 months
LMWH	3.3	37%	21%
Warfarin	7.9	61%	35%
Rivaroxaban	7.9	61%	36%

*Discontinuation was defined as a gap of no more than 60 days between the end of the days of supply of a dispensing and the start date of he next dispensing of the index therapy, if any

Khorana AA *et al*, *Res Pract Thromb Haemost* 2017;1:14–22

Take home message

- ✓ **CAT** đi kèm với nguy cơ tái phát cao và làm **tăng tỷ lệ tử vong** trên bệnh nhân
- ✓ **Rivaroxaban** chứng minh **hiệu quả và an toàn trên BN CAT** thông qua các nghiên cứu pha III và thực tế lâm sàng
- ✓ **Bệnh nhân dễ tuân thủ điều trị** khi dùng rivaroxaban hơn là các kháng đông dạng chích
- ✓ **Nhiều guidelines** quốc tế **khuyến cáo** sử dụng rivaroxaban để điều trị và bảo vệ BN khỏi tái phát VTE

XIN CHÂN THÀNH CẢM ƠN SỰ CHÚ Ý CỦA QUÝ ĐỒNG NGHIỆP

Grade	Benefit vs risk	Quality of evidence
1A	Benefits clearly outweigh risks, or vice versa; recommendation can apply to most patients in most circumstances.	RCTs with no important limitations, or exceptionally strong evidence from observational studies. Further research is unlikely to change our confidence in the estimate of effect.
1B		RCTs with important limitations or strong evidence from observational studies. Further higher-quality research may have an important impact.
1C		At least one critical outcome from RCTs with serious flaws, observational studies, case series, or indirect evidence. Further higher-quality research is likely to have an important impact.
2A	Benefits balanced with risks; best action may differ depending on circumstances or patient/society values.	RCTs with no important limitations, or exceptionally strong evidence from observational studies. Further research is unlikely to change our confidence in the estimate of effect.
2B		RCTs with important limitations or strong evidence from observational studies. Further higher-quality research may have an important impact.
2C	Benefits balanced with risks; other alternatives may be equally reasonable.	At least one critical outcome from RCTs with serious flaws, observational studies, case series, or indirect evidence. Further higher-quality research is likely to have an important impact.

Table II. *ACCP grades for recommendations.*