UASK 2026
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AKCİĞER SAĞLIĞI KONGRESİ
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Sueno Deluxe Hotel, Belek/Antalya
Sizin Sesiniz, Sizin Kongreniz...
ASYOD
AKCİĞER SAĞLIĞI VE YOĞUN BAKIM DERNEĞİ

KANSERLİ HASTALARDA PULMONER TROMBOEMBOLİ YÖNETİMİ

Dr. Nuri Tutar

Erciyes Üniversitesi Tıp Fakültesi Göğüs Hastalıkları AD

- Unprovoked VTE si olan hastalarda malignite olasılığı yaklaşık **%5** dir.
- Malignitesi olan hastalarda VTE olma olasılığı da yaklaşık **%9** dur.
- Son 20 yıl içinde, **kanser hastalarında pıhtı (VTE) görülme sıklığı eski yıllara göre 3 kat artmış.**
- VTE gelişen kanser hastalarında mortalite oranı, VTE'si olmayanlara göre **iki ila üç kat daha fazladır**.

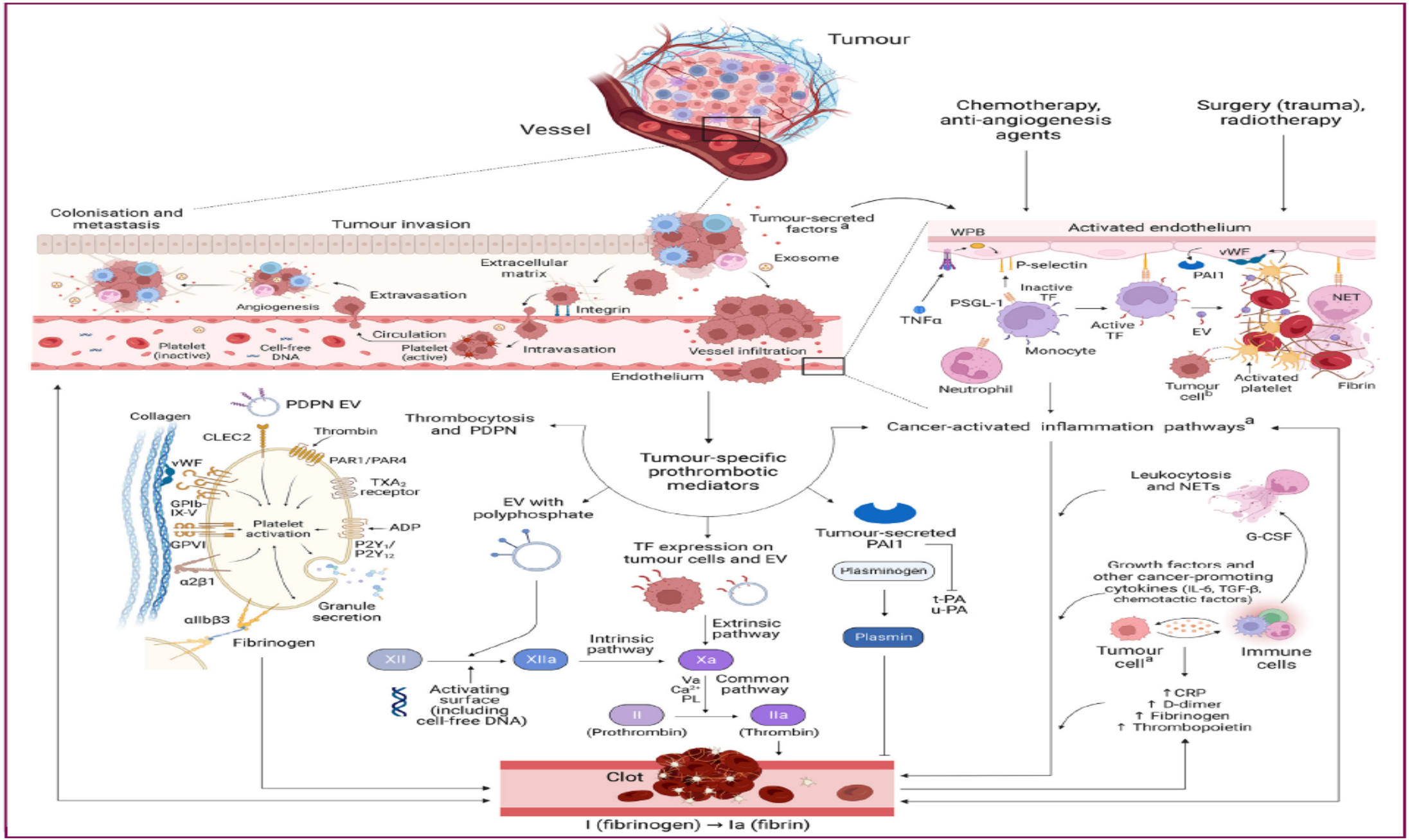
Hemasphere.2019:30:22-23.
Cancer Epidemiol. 2025:95:102764.

- En yüksek VTE oranları, **primer beyin tümörü** olan hastalarda (%47) ve **pankreas** (%19,2), **mide** (%15,8) ve **akciğer** (%13,9) kanseri olan hastalarda gösterilmiştir.
- Hematolojik malignitesi olan hastalar, özellikle **lenfoma** hastaları, da artmış risk altındadır.
- Özellikle ilk tanıdan sonraki **3 ayda** risk daha yüksek.

Eoin D. Oncologist. 2017;22:199-207

- Kanserde venöz tromboemboliye yatkınlık olmasının sebebi hiperkoagülabiliteye yatkınlıktır. Bunlar:
- **Prokoagülan moleküllerin ekspresyonu ve salınımı**,
- **Konakçıya ait kan ve vasküler hücrelerin (yani trombositler, lökositler ve endotelyal hücreler) aktivasyonu**, bu da onların prokoagülan potansiyelini artırır,
- **Antikanser ilaçlar tarafından endotelin aktivasyonu**.

Eoin D. Oncologist. 2017;22:199-207


Tumour
Vessel
Chemotherapy, anti-angiogenesis agents
Surgery (trauma), radiotherapy
Colonisation and metastasis
Tumour invasion
Tumour-secreted factors[a]
Exosome
Extracellular matrix
Integrin
Extravasation
Angiogenesis
Circulation
Platelet (inactive)
Cell-free DNA
Platelet (active)
Intravasation
Vessel infiltration
Endothelium
Activated endothelium
WPB
P-selectin
vWF
PAI1
PSGL-1
Inactive TF
Active TF
EV
NET
TNFα
Monocyte
Neutrophil
Tumour cell[b]
Activated platelet
Fibrin
Cancer-activated inflammation pathways[a]
PDPN EV
Collagen
CLEC2
Thrombin
vWF
PAR1/PAR4
TXA2 receptor
GPIb-IX-V
GPVI
Platelet activation
ADP
P2Y1/P2Y12
α2β1
αIIbβ3
Granule secretion
Fibrinogen
Thrombocytosis and PDPN
Tumour-specific prothrombotic mediators
EV with polyphosphate
TF expression on tumour cells and EV
Tumour-secreted PAI1
Plasminogen
t-PA
u-PA
Plasmin
Leukocytosis and NETs
G-CSF
Growth factors and other cancer-promoting cytokines (IL-6, TGF-β, chemotactic factors)
Tumour cell[a]
Immune cells
↑ CRP
↑ D-dimer
↑ Fibrinogen
↑ Thrombopoietin
XII
XIIa
Intrinsic pathway
Extrinsic pathway
Xa
Va
Ca2+
PL
Common pathway
Activating surface (including cell-free DNA)
II
(Prothrombin)
IIa
(Thrombin)
Clot
I (fibrinogen) → Ia (fibrin)

PROFİLAKSİ KİME?
Khorana risk skorlaması

Parametre	Puan
Çok yüksek riskli kanser türü (mide, pankreas)	2
Yüksek riskli kanser türü (akciğer, lenfoma, jinekolojik, mesane, testis)	1
Trombosit ≥ 350.000/mm³	1
Hemoglobin < 10 g/dL veya EPO kullanımı	1
Lökosit > 11.000/mm³	1
BMI ≥ 35 kg/m²	1

Toplam Puan	Risk
0	Düşük risk
1–2	Orta risk
≥3	Yüksek risk

Çalışma Özelliği	AVERT Çalışması	CASSINI Çalışması
Kullanılan İlaç & Doz	**Apiksaban** (2,5 mg b.i.d.)	**Rivaroksaban** (10 mg o.d.)
Hasta Popülasyonu	**Khorana Skoru ≥ 2**	**Khorana Skoru ≥ 2**
Örneklem Sayısı	574 Hasta	841 Hasta
VTE Oranı (İlaç vs. Plasebo)	**%4,2** vs. %10,2	%6,0 vs. %8,8
Etkinlik (HR)	**0,41**	0,66
Majör Kanama	%3,5 (Plasebo %1,8)	%2,0 (Plasebo %1,0)

DİKKAT: İLAÇ İLAÇ ETKİLEŞİMİ (DOAK VE KANSER İLAÇLARI)

N Engl J Med. 2019;380(8):711-719.
N Engl J Med. 2019;380(8):720-728.

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ANNALS OF ONCOLOGY driving innovation in oncology

SPECIAL ARTICLE

Venous thromboembolism in cancer patients: ESMO Clinical Practice Guideline☆

A. Falanga[1,2], C. Ay[3], M. Di Nisio[4], G. Gerotziafas[5], L. Jara-Palomares[6,7], F. Langer[8], R. Lecumberri[9,10], M. Mandala[11], A. Maraveyas[12], I. Pabinger[3], M. Sinn[8], K. Syrigos[13], A. Young[14] & K. Jordan[15,16], on behalf of the ESMO Guidelines Committee*

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Available online 10 January 2023

Key words: venous thromboembolism (VTE), cancer-associated thrombosis (CAT), thromboprophylaxis/prevention, anticoagulation, catheter-related thrombosis, ESMO Clinical Practice Guideline (CPG)

ASCO special articles

Venous Thromboembolism Prophylaxis and Treatment in Patients With Cancer: ASCO Guideline Update

Nigel S. Key, MBChB[1]; Alok A. Khorana, MD[2]; Nicole M. Kuderer, MD[3]; Kari Bohlke, ScD[4]; Agnes Y.Y. Lee, MD, MSc[5]; Juan I. Arcelus, MD, PhD[6]; Sandra L. Wong, MD, MS[7]; Edward P. Balaban, DO[8]; Christopher R. Flowers, MD, MS[9]; Leigh E. Gates, BA, CPHQ[10]; Ajay K. Kakkar, MD, PhD[11]; Margaret A. Tempero, MD[12]; Shilpi Gupta, MD[13]; Gary H. Lyman, MD, MPH[14]; and Anna Falanga, MD[15]

abstract

PURPOSE To conduct an update of the ASCO venous thromboembolism (VTE) guideline.

METHODS After publication of potentially practice-changing clinical trials, identified through ASCO's signals approach to updating, an updated systematic review was performed for two guideline questions: perioperative thromboprophylaxis and treatment of VTE. PubMed and the Cochrane Library were searched for randomized controlled trials (RCTs) published between November 1, 2018, and June 6, 2022.

RESULTS Five RCTs provided information that contributed to changes to the 2019 recommendations. Two RCTs addressed direct factor Xa inhibitors (either rivaroxaban or apixaban) for extended thromboprophylaxis after surgery. Each of these postoperative trials had important limitations but suggested that these two oral anticoagulants are safe and effective in the settings studied. An additional three RCTs addressed apixaban in the setting of VTE treatment. Apixaban was effective in reducing the risk of recurrent VTE, with a low risk of major bleeding.

RECOMMENDATIONS Apixaban and rivaroxaban were added as options for extended pharmacologic thromboprophylaxis after cancer surgery, with a weak strength of recommendation. Apixaban was also added as an option for the treatment of VTE, with high quality of evidence and a strong recommendation.

Additional information is available at www.asco.org/supportive-care-guidelines.

J Clin Oncol 41:3063-3071.

Table 1. VTE prophylaxis options in cancer patients

Options	Hospitalised patients	Surgical patients	Ambulatory patients
Heparins[a]			
UFH	5000 IU every 8 h	5000 IU 2-4 h preoperatively and every 8 h thereafter	—
Bemiparin	3500 anti-Xa IU o.d.	3500 anti-Xa IU starting 2 h preoperatively or 6 h post-operatively and 3500 anti-Xa IU o.d. thereafter	3500 anti-Xa IU o.d.[b]
Dalteparin	5000 anti-Xa IU o.d.	5000 anti-Xa IU 12 h preoperatively and 5000 anti-Xa IU o.d. thereafter	5000 anti-Xa IU o.d.[b,c]
Enoxaparin	4000 anti-Xa IU o.d.	4000 anti-Xa IU 12 h preoperatively and 4000 anti-Xa IU o.d. thereafter	4000 anti-Xa IU o.d.[b]
Nadroparin	3800 anti-Xa IU o.d. (if weight >70 kg: 5700 anti-Xa IU/kg o.d.)	2850 anti-Xa IU 2-4 h preoperatively and 2850 anti-Xa IU o.d. thereafter	3800 anti-Xa IU o.d. (if weight >70 kg: 5700 anti-Xa IU o.d.)[b]
Tinzaparin	4500 anti-Xa IU o.d.	4500 anti-Xa IU o.d., beginning 12 h post-operatively	4500 anti-Xa IU o.d.[b]
Selective parenteral indirect factor Xa inhibitor			
Fondaparinux	2.5 mg o.d.	2.5 mg o.d. beginning 6-8 h post-operatively	Not studied in the outpatient prophylaxis setting
DOACs			
Apixaban	Not recommended	Not recommended	2.5 mg orally b.i.d.[b]
Rivaroxaban	Not recommended	Not recommended	10 mg orally o.d.[b]
Mechanical prophylaxis			
IPC	If pharmacological VTE prophylaxis is contraindicated[d]	If pharmacological VTE prophylaxis is contraindicated[d]	Not recommended
Venous foot pump	If pharmacological VTE prophylaxis is contraindicated[d]	If pharmacological VTE prophylaxis is contraindicated[d]	Not recommended
GCSs	If pharmacological VTE prophylaxis is contraindicated[d]	If pharmacological VTE prophylaxis is contraindicated[d]	Not recommended

TABLE 1. VTE Recommendations

Clinical Question	Recommendations	Type; Evidence Quality; Strength of Re
1. Should hospitalized patients with cancer receive anticoagulation for VTE prophylaxis?	1.1. Hospitalized patients who have active malignancy and acute medical illness or reduced mobility should be offered pharmacologic thromboprophylaxis in the absence of bleeding or other contraindications	Type: Evidence based Evidence quality: Intermediate Strength of recommendation: Moderat
	1.2. Hospitalized patients who have active malignancy without additional risk factors may be offered pharmacologic thromboprophylaxis in the absence of bleeding or other contraindications	Type: Evidence based Evidence quality: Low Strength of recommendation: Moderat
	1.3. Routine pharmacologic thromboprophylaxis should not be offered to patients admitted for the sole purpose of minor procedures or chemotherapy infusion nor to patients undergoing stem-cell/bone marrow transplantation	Type: Informal consensus Evidence quality: Insufficient Strength of recommendation: Moderat
2. Should ambulatory patients with cancer receive anticoagulation for VTE prophylaxis during systemic chemotherapy?	2.1. Routine pharmacologic thromboprophylaxis should not be offered to all outpatients with cancer	Type: Evidence based Evidence quality: Intermediate to High Strength of recommendation: Strong
	2.2. High-risk outpatients with cancer (Khorana score of 2 or higher before starting a new systemic chemotherapy regimen) may be offered thromboprophylaxis with apixaban, rivaroxaban, or LMWH provided there are no significant risk factors for bleeding and no drug interactions. Consideration of such therapy should be accompanied by a discussion with the patient about the relative benefits and harms, drug cost, and duration of prophylaxis in this setting	Type: Evidence based Evidence quality: Intermediate to High and rivaroxaban, Intermediate for L Strength of recommendation: Moderat
	2.3. Patients with multiple myeloma receiving thalidomide- or lenalidomide-based regimens with chemotherapy and/or dexamethasone should be offered pharmacologic thromboprophylaxis with either aspirin or LMWH for lower-risk patients and LMWH for higher-risk patients	Type: Evidence based Evidence quality: Intermediate Strength of recommendation: Strong

Durum	ASCO 2023 Temel Öneri	ESMO 2023 Temel Öneri	Profilaksi Süresi
Cerrahi Profilaksi	LMWH/UFH standart. Uzatılmış profilakside DOAC (Zayıf Öneri/Düşük Kanıt) eklendi.	LMWH/UFH standart (En yüksek profilaktik doz vurgusu).	7-10 gün (Majör vakalarda 4 haftaya uzatılır)
Ambulatuvar (Ayaktan)	Khorana ≥ 2 ise Doğrudan Faktör Xa İnhibitörü veya LMWH.	Khorana ≥ 2 veya Vienna-CATS/COMPASS-CAT ile yüksek risk saptanması.	Tedavi süresince (Genellikle 6 aya kadar)
Pankreas Kanseri	Khorana odaklı standart profilaktik dozlar.	Yüksek doz LMWH (Dalteparin 150 IU/kg / Enoksaparin 1 mg/kg).	İlk 3 ay
Multipl Miyelom	IMiD kullanımına göre Aspirin veya LMWH.	IMWG/NCCN skoruna göre düşük riskte Aspirin; yüksek riskte LMWH veya DOAC.	3-6 ay
Böbrek Yetmezliği	CrCl < 30 ml/min ise parenteral ajanlar tercih edilir.	CrCl < 15 ml/min ise DOAC kontrendike; CrCl 15-30 arası veri kısıtlı.	Klinik duruma göre

KANSER HASTALARINDA VTE TEDAVİSİ

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Low-Molecular-Weight Heparin versus a Coumarin for the Prevention of Recurrent Venous Thromboembolism in Patients with Cancer

Agnes Y.Y. Lee, M.D., Mark N. Levine, M.D., Ross I. Baker, M.D., Chris Bowden, M.D., Ajay K. Kakkar, M.B., Martin Prins, M.D., Frederick R. Rickles, M.D., Jim A. Julian, M.Math., Susan Haley, B.Sc., Michael J. Kovacs, M.D., and Michael Gent, D.Sc., for the Randomized Comparison of Low-Molecular-Weight Heparin versus Oral Anticoagulant Therapy for the Prevention of Recurrent Venous Thromboembolism in Patients with Cancer (CLOT) Investigators*

ABSTRACT

BACKGROUND

Patients with cancer have a substantial risk of recurrent thrombosis despite the use of oral anticoagulant therapy. We compared the efficacy of a low-molecular-weight heparin with that of an oral anticoagulant agent in preventing recurrent thrombosis in patients with cancer.

METHODS

Patients with cancer who had acute, symptomatic proximal deep-vein thrombosis, pulmonary embolism, or both were randomly assigned to receive low-molecular-weight heparin (dalteparin) at a dose of 200 IU per kilogram of body weight subcutaneously once daily for five to seven days and a coumarin derivative for six months (target international normalized ratio, 2.5) or dalteparin alone for six months (200 IU per kilogram once daily for one month, followed by a daily dose of approximately 150 IU per kilogram for five months).

RESULTS

During the six-month study period, 27 of 336 patients in the dalteparin group had recurrent venous thromboembolism, as compared with 53 of 336 patients in the oral-anticoagulant group (hazard ratio, 0.48; P=0.002). The probability of recurrent thromboembolism at six months was 17 percent in the oral-anticoagulant group and 9 percent in the dalteparin group. No significant difference between the dalteparin group and the oral-anticoagulant group was detected in the rate of major bleeding (6 percent and 4 percent, respectively) or any bleeding (14 percent and 19 percent, respectively). The mortality rate at six months was 39 percent in the dalteparin group and 41 percent in the oral-anticoagulant group.

CONCLUSIONS

In patients with cancer and acute venous thromboembolism, dalteparin was more effective than an oral anticoagulant in reducing the risk of recurrent thromboembolism without increasing the risk of bleeding.

Table 2. Sites of Solid Tumors.

Tumor Site	Dalteparin (N=298)	Oral Anticoagulant (N=308)
	no. of patients	
Breast	59	49
Colorectal area	54	54
Lung	40	50
Genitourinary tract	39	47
Gynecologic system	38	30
Pancreas	13	16
Brain	14	13
Other	41	49

Table 3. Primary Efficacy Outcome Events.

Event	Dalteparin (N=336)	Oral Anticoagulant (N=336)
	no. of patients	
Deep-vein thrombosis alone	14	37
Nonfatal pulmonary embolism	8	9
Fatal pulmonary embolism	5	7
Total	27	53

Sonuç olarak Dalteparin, warfarine göre kanser ve VTE hastalarında kanama oranını arttırmadan (%6-%4) nüksü daha iyi önlediği gösterilmiş.

Published in final edited form as:
Thromb Res. 2015 September 01; 136(3): 582–589. doi:10.1016/j.thromres.2015.07.011.

Treatment of Venous Thromboembolism in Patients with Cancer: A Network Meta-Analysis Comparing Efficacy and Safety of Anticoagulants

Florian Posch, MD MSc[1], Oliver Königsbrügge, MD[1], Christoph Zielinski, MD[2], Ingrid Pabinger, MD[1], Cihan Ay, MD[1]

Study acronym	CANTHANOX	CLOT	ONCENOX	LITE	Romera et al.	CATCH
First Author (Year of publication)[Ref.]	Meyer G (2002)[29]	Lee AYY (2003) [30]	Deitcher SR (2006) [28]	Hull RD (2007) [31]	Romera A (2008) [32]	Lee AYY (2014) [22]
Study type* (Publication status)	CPST (Full Report)	CPST (Full Report)	CPST (Full Report)	SA (Full Report)	SA (Full Report)	CPST (Abstract)
Intervention	LMWH (Enoxaparin)	LMWH (Dalteparin)	LMWH (Enoxaparin)	LMWH (Tinzaparin)	LMWH (Tinzaparin)	LMWH (Tinzaparin)
Comparator	VKA (Warfarin)	VKA (Any type)	VKA (Warfarin)	VKA (Any type)	VKA (Aceno-coumarol)	VKA (Warfarin)
Follow-up time†	3 months	6 months	6 months	3 months	6 months	6 months
Number of recurrent VTE events in intervention group (N total)	2 (71)	27 (336)	4 (61)	6 (100)	2 (36)	31 (449)
Number of recurrent VTE events in comparator group (N total)	3 (75)	53 (336)	3 (30)	10 (100)	3 (33)	45 (451)
Number of major bleedings in intervention group (N total)	5 (71)	19 (338)	6 (67)	7 (100)	N/A	13 (449)
Number of major bleedings in comparator group (N total)	12 (75)	12 (335)	1 (34)	7 (100)	N/A	12 (451)
Cancer status definition	Patients with solid or hematologic cancers, either active or in remission with ongoing antitumor treatment (no definition of active cancer reported)	Patients with active cancer (defined as recurrent or meta-static cancers, or cancer diagnosis or treatment within 6 months	Patients not being candidates for curative surgery with active cancer (defined as measurable disease or histo-cyto-logical diagnosis ± elevated tumor markers)	No specific definition reported	No specific definition reported	Patients with active cancer (no specific definition of active cancer reported)

🔎 Etkinlik (Rekürren VTE açısından)

- **RR = 0.60**
- **%95 GA: 0.45–0.79**
- **p < 0.001**

Bu, **LMWH'nin (Low Molecular Weight Heparin)**, **VKA'ya (Vitamin K Antagonistleri)** kıyasla **rekürren venöz tromboembolizm (VTE)** riskini yaklaşık %40 oranında azalttığını** gösterir.

- RR'nin 1'in altında olması → LMWH lehine anlamlı risk azalımı
- Güven aralığının (0.45–0.79) 1'i kesmemesi → istatistiksel olarak anlamlı
- p<0.001 → güçlü istatistiksel anlamlılık

📌 **Klinik anlamı:** Özellikle kanser ilişkili VTE'de LMWH, nüksü önlemede VKA'dan daha etkilidir.

🩸 Güvenlik (Majör kanama açısından)

- **RR = 1.08**
- **%95 GA: 0.70–1.66**
- **p = 0.74**
- RR 1'e çok yakın → iki tedavi arasında anlamlı fark yok
- Güven aralığı 1'i içeriyor → istatistiksel olarak anlamlı değil
- p=0.74 → fark yok

📌 **Klinik anlamı:** LMWH, kanama riski açısından VKA'ya benzer güvenlik profiline sahiptir.

DOAK’lar

- DMAH etkili ancak uygulaması zor,
- DMAH maliyetleri yüksek
- DOAK lar VTE de etkili görülüyor ancak kanserli VTE hastlarında kullanılabilir mi?

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Edoxaban for the Treatment of Cancer-Associated Venous Thromboembolism

Gary E. Raskob, Ph.D., Nick van Es, M.D., Peter Verhamme, M.D., Marc Carrier, M.D., Marcello Di Nisio, M.D., David Garcia, M.D., Michael A. Grosso, M.D., Ajay K. Kakkar, M.B., B.S., Michael J. Kovacs, M.D., Michele F. Mercuri, M.D., Guy Meyer, M.D., Annelise Segers, M.D., Minggao Shi, Ph.D., Tzu-Fei Wang, M.D., Erik Yeo, M.D., George Zhang, Ph.D., Jeffrey I. Zwicker, M.D., Jeffrey I. Weitz, M.D., and Harry R. Büller, M.D., for the Hokusai VTE Cancer Investigators*

N Engl J Med 2018;378:615-24.

1046 hasta

Edoksaban 60 1x1 vs
Dalteparin 200-150 IU/kg

Nüks: %7.9 vs %11.3
Major kanama %6.9 vs %4

Major kanamayı arttıran sebep GIS tümörü hastaları

VOLUME 36 · NUMBER 20 · JULY 10, 2018

JOURNAL OF CLINICAL ONCOLOGY

RAPID COMMUNICATION

Comparison of an Oral Factor Xa Inhibitor With Low Molecular Weight Heparin in Patients With Cancer With Venous Thromboembolism: Results of a Randomized Trial (SELECT-D)

Annie M. Young, Andrea Marshall, Jenny Thirlwall, Oliver Chapman, Anand Lokare, Catherine Hill, Danielle Hale, Janet A. Dunn, Gary H. Lyman, Charles Hutchinson, Peter MacCallum, Ajay Kakkar, F.D. Richard Hobbs, Stavros Petrou, Jeremy Dale, Christopher J. Poole, Anthony Maraveyas, and Mark Levine

1046 hasta

Rivaroksaban 15 2x1 – 20 1x1
vs Dalteparin 200-150 IU/kg

Nüks: %4 vs %11
Major kanama %6 vs %4

Major kanamayı arttıran sebep yine GIS tümörü hastaları

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journal homepage: www.elsevier.com/locate/ajc

Expert review

Direct Oral Anticoagulants Versus Low-Molecular-Weight Heparin in Patients With Cancer-Associated Thrombosis: A Meta-Analysis of Randomized Controlled Trials

Asma Mousavi, MD[a,b], Shayan Shojaei, MD[a,b*], Soheil Rahmati, MD[a], Parham Dastjerdi, MD[a,c], Mahshad Sabri, MD[d], Keyvan Salehi, MD[a,e], Kasra Izadpanahi, MD[a,b], Homayoun Pishraft-sabet, MD[a,b], Elmira Jafari Afshar, MD[f], Mahsa Noohi Arbatan, MD[b], Marc Samsky, MD[g], Kolte Dhaval, MD[h], Jamal Rana, MD[i], Toshiki Kuno, MD[h], Jay Giri, MD[j], Kaveh Hosseini, MD[a]

[a] *Tehran Heart Center, Cardiovascular Diseases Research Institute, Tehran University of Medical Sciences, Tehran, Iran*

Kanser İlişkili Tromboz Tedavisi: DOAK ve DAAH Karşılaştırması

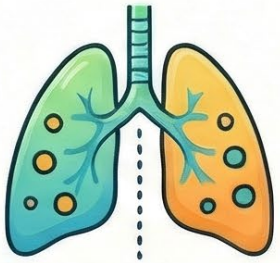
4.713 katılımcıyı kapsayan 10 randomize kontrollü çalışmayı (RCT) incelemektedir. Çalışma, kanser hastalarında tekrarlayan pıhtılaşma olaylarını önlemede ağızdan alınan DOAK'ların (Apixaban, Rivaroxaban vb.) geleneksel iğne tedavisi olan DAAH (Dalteparin vb.) ile karşılaştırıldığında ne kadar başarılı ve güvenli olduğunu belirlemektir.

Klinik Etkinlik ve VTE Önleme

%34

Tekrarlayan VTE Riskinde %34 Azalma

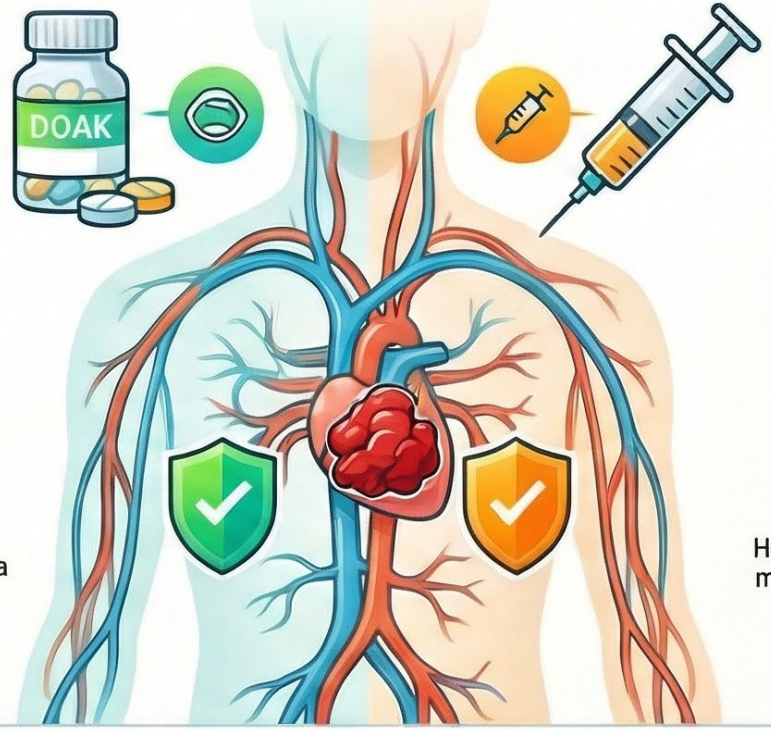
DOAK kullanımı, DAAH'ye kıyasla venöz tromboembolizm (VTE) riskini anlamlı derecede daha fazla azaltmaktadır.

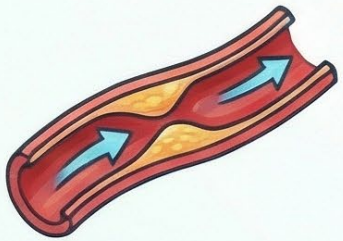


DOAK DAAH

Benzer Pulmoner Emboli Oranları

Akciğer embolisi (PE) riskini azaltma konusunda her iki tedavi yöntemi benzer etkinlik göstermiştir.





Üstün DVT Koruması

DOAK'lar, tekrarlayan derin ven trombozu (DVT) vakalarını önlemede DAAH'ye göre daha etkili sonuçlar sergilemiştir.

Güvenlik Profili ve Sağkalım

Majör Kanama Oranları Eşit

Her iki tedavi grubunda da ciddi majör kanama riski istatistiksel olarak benzer düzeydedir.

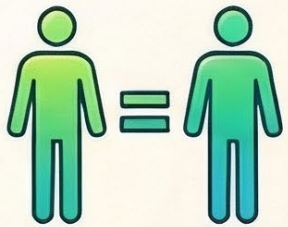
DOAK DAAH

Daha Yüksek KAMOK Riski

Klinik olarak anlamlı majör olmayan kanama (KAMOK) olayları, DOAK kullanan hastalarda daha sık görülmektedir.

Temel Sonuçların İnsidans Risk Oranı (İRO) Karşılaştırması

Klinik Sonuç	İRO (DOAK vs. DAAH)	Klinik Yorum
Tekrarlayan VTE	0.66	✓ DOAK belirgin şekilde daha etkili
Majör Kanama	1.00	= Tedaviler arasında fark yok
KAMOK (Kanama)	1.68	✓ DAAH daha güvenli

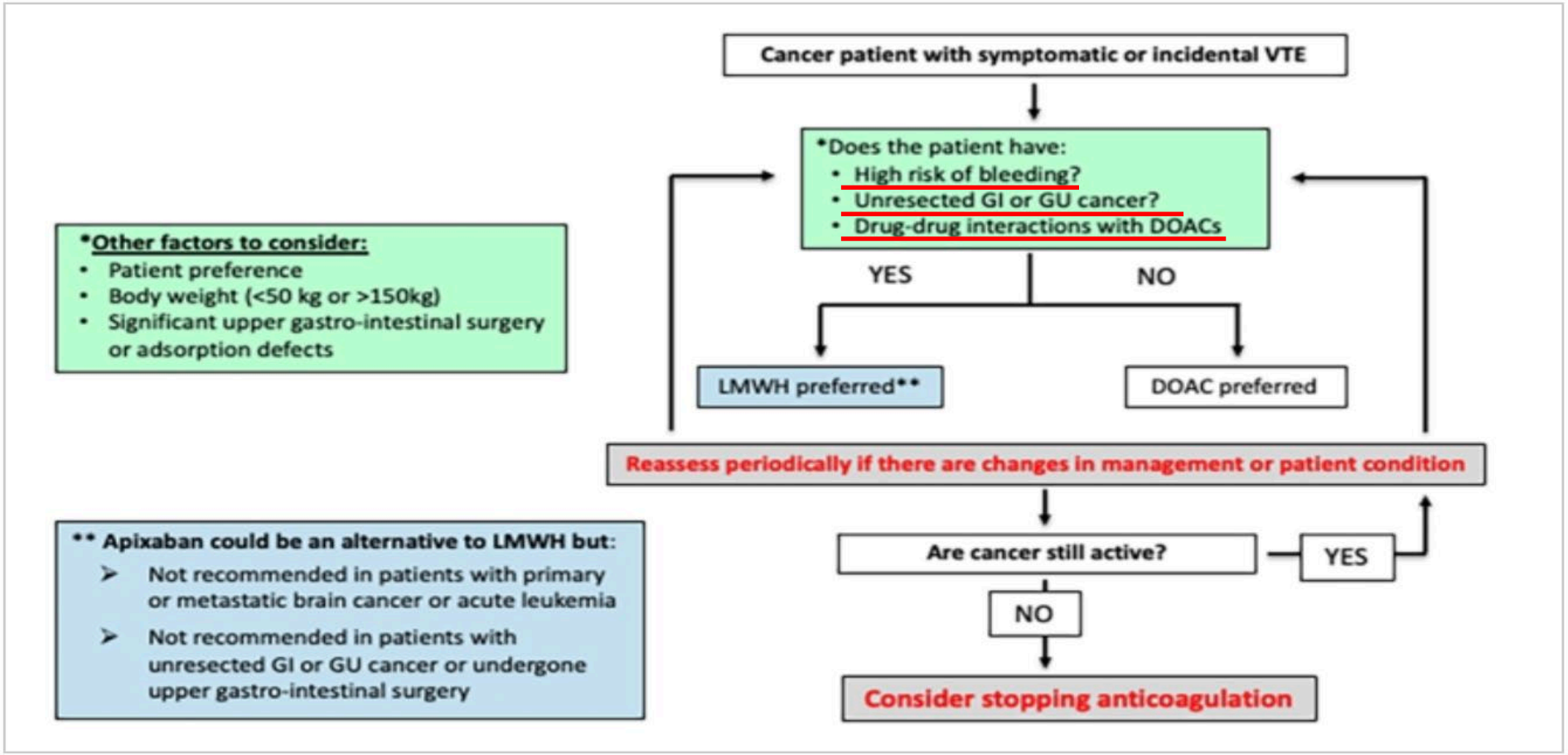


Değişmeyen Mortalite Oranı

Tedavi seçimi, hastaların genel sağkalımı veya tüm nedenlere bağlı ölüm oranları üzerinde bir fark yaratmamıştır.

KANSER HASTALARINDA PTE TEDAVİSİ

Figure 1. Algorithm for the treatment of cancer-associated venous thromboembolism.



ESC European Society of Cardiology

DOAC: direct oral anticoagulants; GI: gastrointestinal; GU: genitourinary; LMWH: low-molecular-weight heparin; VTE: venous thromboembolism

Table 3 Guideline Recommendations for the Treatment of Cancer-Associated VTE

Guideline	Recommendations	
	Initial Treatment	**Treatment Duration**

ACCP[a]	• Apixaban, edoxaban or rivaroxaban (strong recommendation)
	  ○ Apixaban or LMWH may be preferred in luminal GI malignancies.
		• Extended-phase DOAC therapy (>3 months)
		  ○ Reassess periodically.

	• DOAC (apixaban or rivaroxaban) or LMWH (conditional recommendation)
	  ○ Caution with DOACs in GI cancers.
		• Treat for 3–6 months with a DOAC (apixaban, edoxaban or rivaroxaban) over LMWH or VKA (conditional recommendations).
		• Treat for >6 months rather than short term (3–6 months) in patients with active cancer (conditional recommendation).
		  ○ Suggest continuing indefinitely rather than stopping after completion of a definitive period of anticoagulation (conditional recommendation).
		  ○ Use a DOAC or LMWH (conditional recommendation).

NCCN[a]	• Apixaban (category 1), edoxaban after ≥5 days of parenteral anticoagulation (category 1) or rivaroxaban (category 2A) preferred for patients without gastric or gastroesophageal lesions ○ Caution in GU tract lesions • LMWH preferred for patients with gastric or gastroesophageal lesions (category 1). • Dabigatran if above regimens are not appropriate or unavailable.	• ≥3 months or as long as active cancer or cancer therapy.

ASCO[b]	• LMWH, UFH, fondaparinux, rivaroxaban, or apixaban
	  ○ For long-term anti-coagulation, LMWH, edoxaban, rivaroxaban, or apixaban for at least 6 months are preferred over VKAs. Caution with direct factor Xa inhibitors in patients with GI and GU cancers or other high-risk settings.
		• Offer LMWH, DOACs or VKAs beyond the initial 6 months to select patients with active cancer, such as those with metastatic disease or those receiving chemotherapy.
		  ○ LMWH, edoxaban or rivaroxaban preferred.
		  ○ LMWH preferred in settings with increased bleeding risk.
		• Assess intermittently to ensure a continued favorable risk-benefit profile.
		• Patients needing extended pharmacologic antithrombotic prophylaxis post cancer surgery
		  ○ Prophylactic doses of LMWH

ESC[b]	• PE and cancer: LMWH for the first 3–6 months (IIa. A) • Edoxaban (IIa. B) or rivaroxaban (IIa. C) may be used except in GI cancer patients.	• Extend indefinitely or until the cancer is cured (IIa. B). • Consider LMWH, DOAC or VKA.
ITAC[b]	• LMWH when CrCl ≥30 mL/min (grade 1A). • Apixaban or rivaroxaban (first 10 days) or edoxaban (started after initial LMWH/UFH for 5 days) can be used for initial treatment if CrCl ≥30 mL/min and patient is not at high risk of GI or GU bleeding (grade 1 A).	• LMWH or DOACs for ≥6 months (grade 1 A) ○ DOACs when CrCl ≥30 mL/min if no impairment in GI absorption or strong DDIs (grade 1 A), but caution advised in GI malignancies, especially upper GI tract. • After 6 months, termination or continuation of anticoagulation based on benefit–risk ratio, tolerability, drug availability, patient preference and cancer activity (guidance).
ISTH[b]	• Patients with low bleeding risk and no DDIs: edoxaban or rivaroxaban; LMWHs are acceptable alternatives. • Patients with high bleeding risk[c]: LMWH; edoxaban or rivaroxaban as an alternative if no potential DDI.	• No specific recommendation.

(*Continued*)

Table 3 (Continued).

Guideline	Recommendations	
	Initial Treatment	**Treatment Duration**
NICE[b]	• Consider DOAC if active cancer and confirmed proximal DVT or PE. • If DOAC unsuitable, consider LMWH alone or VKA (following initial LMWH). • Choice of anticoagulant should consider tumor site, DDIs and bleeding risk.	• Review treatment at 3 to 6 months according to clinical need.

ESMO	• During the acute phase (first 5–10 days after diagnosis)
	  ○ Consider LMWH, UFH, fondaparinux, apixaban or rivaroxaban (I, A)
	  ○ LMWH is preferable to UFH and fondaparinux (V, A)
		• For long-term anticoagulation for at least 6 months
		  ○ LMWH, apixaban, edoxaban or rivaroxaban are preferred to VKAs (I, A)
		  ○ In patients with luminal GI cancer, urothelial cancer (II, B), patients at high risk of GI bleeding, receiving powerful inducers and/or inhibitors of CYP3A4 or P-gp, (IV, B) LMWH is preferred.
		• Beyond initial 6 months, LMWH, apixaban, edoxaban, rivaroxaban or VKAs based on benefit–risk assessment (III, B)
		• Regularly assess risk–benefit profile of anticoagulation therapy for favorable balance (IV, C)

Notes: This table collates data from the cited published papers,[31,37–42,69,72] also over viewed in two previously published studies[55,56] and new data available since then. [a]Recommendations based on ADAM VTE, Caravaggio, Hokusai VTE Cancer and SELECT-D trial results. [b]Recommendations based on Hokusai VTE Cancer and SELECT-D trial results. [c]High bleeding risk includes patients with luminal gastrointestinal cancers with an intact primary; cancers at risk of bleeding from the genitourinary tract, bladder, or nephrostomy tubes; or active GI mucosal abnormalities (eg, duodenal ulcers, gastritis, esophagitis, or colitis).

Abbreviations: ACCP, American College of Chest Physicians; ASCO, American Society of Clinical Oncology; CrCl, creatinine clearance; CYP3A4, cytochrome P450 3A4; DDI, drug–drug interaction; DOAC, direct oral anticoagulant; ESC, European Society of Cardiology; ESMO, European Society for Medical Oncology; GI, gastrointestinal; GU, genitourinary; ISTH, International Society on Thrombosis and Haemostasis; ITAC, International Initiative on Thrombosis and Cancer; LMWH, low-molecular-weight heparin; NICE, National Institute for Health and Care Excellence; NCCN, National Comprehensive Cancer Network; P-gp, P-glycoprotein; PE, pulmonary embolism; UFH, unfractionated heparin; VKA, vitamin K antagonist; VTE, venous thromboembolism.

Kanser İlişkili VTE Tedavi Rehberleri Özet Tablosu

Rehber	Başlangıç Tedavisi (0-6 Ay)	Süre / Kritik Not
ACCP (2021)	**DOAK** (Apiksaban, edoksaban, rivaroksaban)	>3 ay. Periyodik değerlendirme.
ASH (2021)	**DOAK** önerilir. Gİ kanserinde DMAH.	>6 ay (Aktif kanserde süresiz).
NCCN (2023)	Gİ dışı: **DOAK**. Gİ kanseri: **DMAH**.	≥3 ay veya kanser sürdükçe.
ASCO (2023)	**DOAK veya DMAH**. Gİ/GÜ'de dikkat.	>6 ay. Kanama riskinde **DMAH**.
ESC (2019)	PE varsa ilk 3-6 ay **DMAH**. Gİ dışı: **DOAK**.	Kanser kür olana kadar süresiz.
ITAC (2022)	CrKl ≥30 ise **DOAK**. Gİ/GÜ riskte **DMAH**.	≥6 ay. 6. ayda risk/fayda analizi.
ISTH (2022)	Düşük riskte **DOAK**, yüksek riskte **DMAH**.	Klinik duruma göre bireysel karar.
NICE (2023)	Önce **DOAK**. Uygun değilse **DMAH**.	3. ve 6. aylarda gözden geçirme.
ESMO (2023)	**DOAK veya DMAH**. Gİ/Ürotelyal: **DMAH**.	>6 ay. Aktif kanserde devam.

Tablo 4: Zorlayıcı Kanser Alt Gruplarında VTE Tedavisi İçin Ö

Kanser Alt Grubu	Önerilen Antikoagülan Tedavi
Gastrointestinal Kanserler	• **Apiksaban**, özellikle alt gastr hastalarda bir seçenek olabilir.
	• Rezeke edilmemiş üst gastroi hastalarda **DMAH** tercih edilen
	• Gastrointestinal kanserli hast artmış Gİ kanama riski akılda tu
Genitoüriner Kanserler	• **DMAH veya DOAK** kullanılab
	• Aktif mesane lezyonu olan ve hastalarda **DMAH** tercih edilen
Beyin Tümörleri (Primer veya Metastatik)	• **DOAK veya DMAH** kullanılab
	• DOAK'ların, özellikle apiksaba hemoraji riskini artırdığı gösteri

Tablo 4: Zorlayıcı Kanser Alt Gruplarında VTE Tedavisi (Özet)

Durum / Kanser Alt Grubu	Önerilen Antikoagülan Tedavi
Trombositopeni	• **Trombosit sayısı >50 × 10^9/L:** Tam doz DOAK .
	• **Trombosit sayısı 25–50 × 10^9/L:** Doz ayarlı DMAH (tercih edilen) veya yarı doz DOAK (apiksaban, edoksaban veya rivaroksaban) .
	• **Trombosit sayısı <25 × 10^9/L:** Antikoagülasyonu durdurun.
Böbrek Yetmezliği	• **CrCl $\geq$30 mL/dakika:** apiksaban, edoksaban (CrCl 30–50 mL/dakika için yarı doz) veya rivaroksaban .
	• **CrCl <30 mL/dakika:** doz ayarlı DMAH (anti-Xa seviyesi takibi ile) veya apiksaban düşünün (CrCl <25 mL/dakika olmadığı sürece).

KANSERDE HANGİ DOAK?

Outcomes		Major bleeding, %	Recurrent VTE, %	All causes mortality, %
Meyer 2002 (CANTHANOX)	Enoxaparin (n=71)	3m: 7%	3m: 2.8%	31%
	Warfarin (n=75)	3m: 16%	3m: 4%	38.7%
Lee 2003 (CLOT)	Dalteparin (n=338)	6%	9%	38.5%
	VKA (n=338)	4%	17%	40.2%
ONCENOX 2006	Enoxaparin (n=36)	11.1%	6.3%	41.7%
	Warfarin (n=34)	2.9%	10%	32.4%
CATCH 2015	Tinzaparin (n=449)	2.7%	6.9%	33.4%
	Warfarin (n=451)	2.4%	10%	30.6%
SELECT-D 2018	Rivaroxaban (n=203)	6%	4%	25%
	Dalteparin (n=203)	4%	11%	30%
Raskob 2018 (HOKUSAI VTE Cancer)	Edoxaban (n=522)	6.9%	7.9%	39.5%
	Dalteparin (n=524)	4%	11.3%	36.6%*
ADAM VTE 2020	Apixaban (n=150)	0%	0.7%	16%
	Dalteparin (n=150)	1.4%	6.3%	11%
CARAVAGGIO trial 2020	Apixaban (n=576)	3.8%	5.6%	23.4%
	Dalteparin (n=576)	4%	7.9%	26.4%

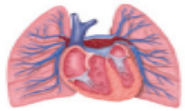
JACC: CARDIOONCOLOGY VOL. 6, NO. 1, 2024

ORIGINAL RESEARCH

Comparing Anticoagulation Strategies for Venous Thromboembolism Associated With Active Cancer

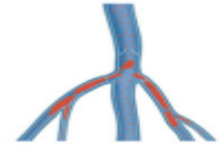
A Systematic Review and Meta-Analysis

Tomohiro Fujisaki, MD,[a,b] Daisuke Sueta, MD, PhD,[a] Eiichiro Yamamoto, MD, PhD,[a] Conor Buckley, MD,[c] Guilherme Sacchi de Camargo Correia, MD,[d] Julia Aronson, MD,[e] Paulino Tallón de Lara, MD, PhD,[f] Koichiro Fujisue, MD, PhD,[a] Hiroki Usuku, MD, PhD,[a] Kenichi Matsushita, MD, PhD,[a] Roxana Mehran, MD,[g] George D. Dangas, MD, PhD,[g] Kenichi Tsujita, MD, PhD[a]



Pulmonary embolism

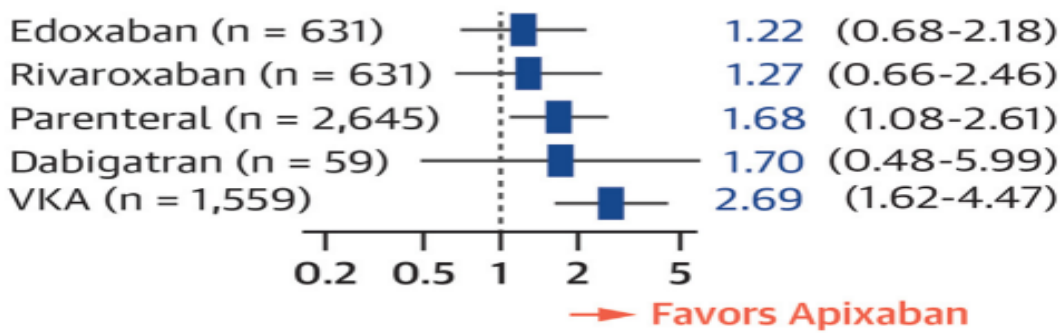
Meta-analysis of 17 studies of patients with active cancer (N = 6,623)



Deep vein thrombosis

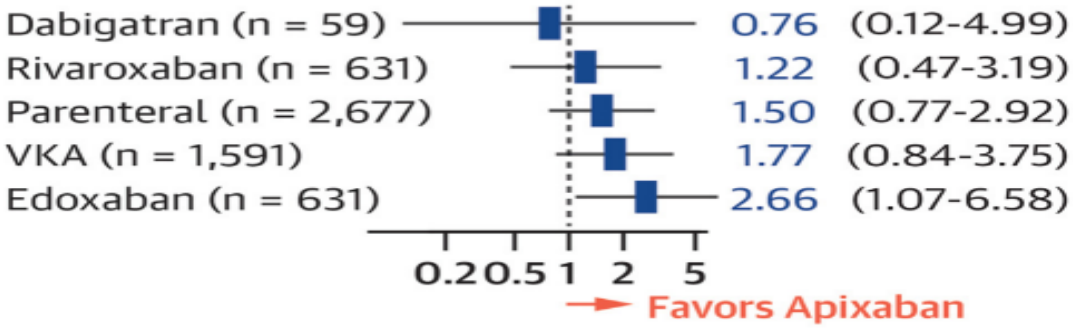
Primary Efficacy Outcome: Recurrent VTE (DVT, PE)

Other Anticoagulant vs Apixaban (n = 852)



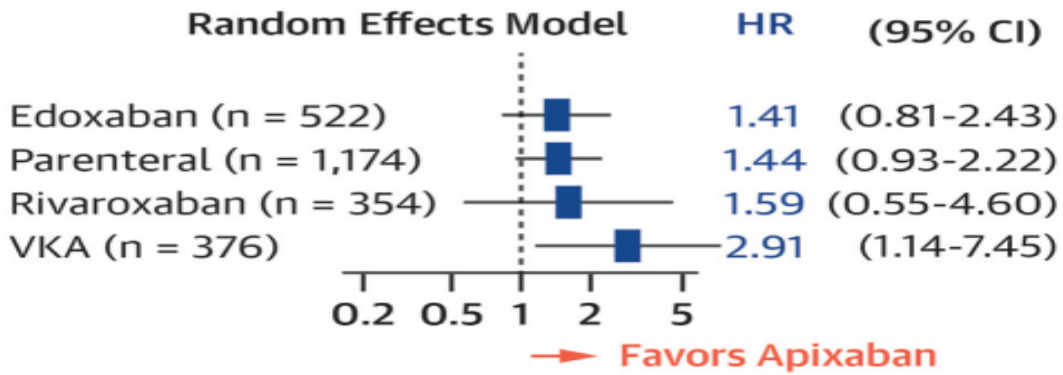
Primary Safety Outcome: Major Bleeding

Other Anticoagulant vs Apixaban (n = 852)



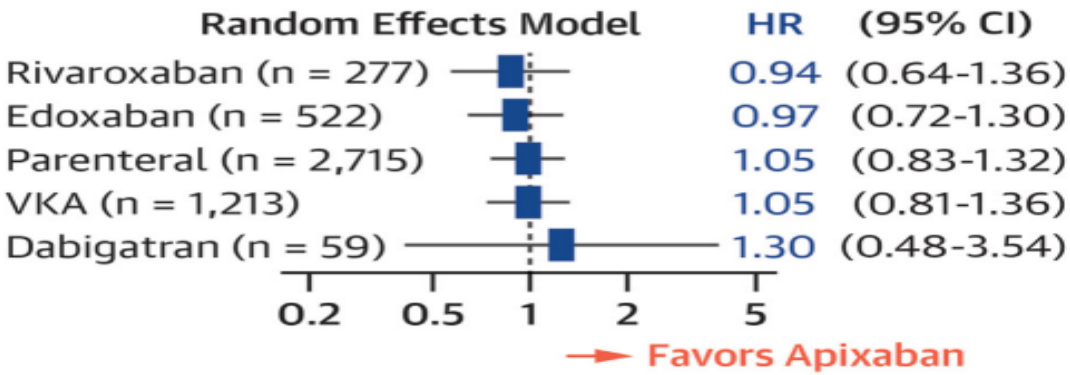
Net Adverse Clinical Outcome: VTE or Major Bleeding

Other Anticoagulant vs Apixaban (n = 576)



All-Cause Death

Other Anticoagulant vs Apixaban (n = 871)



Fujisaki T, et al. J Am Coll Cardiol CardioOnc. 2024;6(1):99–113.

Kanserde Embolinin Uzun Süreli Tedavisi

- Kanser hastalarında **malignitede kür saptanana kadar ya da süresiz** antikoagülasyon önerilir (Kanıt 2aB)
- Kanser hastasında kür saptandığı zaman tedavinin kesilmesi düşünülebilir. Fakat kür kavramı kanserde göreceli olabilmektedir.

Kanser ilişkili VTE tedavisinde;

- Bireyselleştirilmiş tedavi (ilaç etkileşimi, kanama riski)
- ***Monoterapi (kombine antitrombotiklerdense)***
- İnsidental VTE, nüks riski nedeniyle tedavi edilmesi
- ***3-6 ay tedavi, ancak aktif kanser olduğu sürece tedaviye devam edilmesi***

Kanser Hastalarında Azaltılmış Dozla Uzun Süreli Tedavi

The NEW ENGLAND JOURNAL of MEDICINE

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Extended Reduced-Dose Apixaban for Cancer-Associated Venous Thromboembolism

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ABSTRACT

- **Apixaban** 2.5 mg 2x1 ile, 5 mgr 2x1 karşılaştırılıyor.
- **En az 6 ay** DMAH-DOAK-Warfarin alan hastalar çalışmaya alınıyor.
- Nüks VTE birincil sonlanım noktası olarak belirlenmiş.
- **1766 hasta** çalışmaya alınmış.
- Ortalama takip süresi **11.8 ay**.

Outcome	Reduced-Dose Apixaban (N = 866)	Full-Dose Apixaban (N = 900)	Treatment Effect (95% CI)	P Value
	number (percent)			
Primary efficacy outcome: recurrent venous thromboembolism†	18 (2.1)	24 (2.8)	0.76 (0.41–1.41)	0.001
Recurrent symptomatic venous thromboembolism	17 (2.0)	18 (2.1)	0.97 (0.50–1.88)	—
Lower-limb deep-vein thrombosis‡	8 (0.9)	6 (0.7)	—	
Pulmonary embolism	9 (1.1)	10 (1.2)	—	
Fatal pulmonary embolism	0	0	—	
Unexplained sudden death§	3 (0.4)	2 (0.3)	—	
Upper-limb deep-vein thrombosis	1 (0.1)	3 (0.4)	—	
Central venous catheter–related thrombosis	1 (0.1)	2 (0.2)	—	
Incidental venous thromboembolism¶	1 (0.1)	6 (0.7)	—	
Recurrent major venous thromboembolism‖	17 (2.0)	21 (2.4)	0.83 (0.44–1.57)	—
Key secondary safety outcome: major or clinically relevant nonmajor bleeding**	102 (12.1)	136 (15.6)	0.75 (0.58–0.97)	0.03
Major bleeding	24 (2.9)	37 (4.3)	0.66 (0.40–1.10)	—
Fatal bleeding	2 (0.2)	2 (0.2)	—	
Major gastrointestinal bleeding	12 (1.4)	25 (2.9)	—	
Upper gastrointestinal bleeding	6 (0.7)	13 (1.5)	—	
Lower gastrointestinal bleeding	7 (0.8)	13 (1.5)	—	
Clinically relevant nonmajor bleeding	84 (10.0)	107 (12.3)	0.79 (0.59–1.05)	

- Bu çalışma şunları göstermektedir:
- Aktif kanserli hastalarda tekrarlayan venöz tromboembolizmin önlenmesinde, düşük doz apixaban ile uzun süreli antikoagülasyon, tam doz apixaban ile karşılaştırıldığında **daha düşük etkili değildir.**
- Düşük doz, tam doza kıyasla klinik olarak **anlamlı kanama komplikasyonlarının daha düşük insidansına** yol açmıştır.

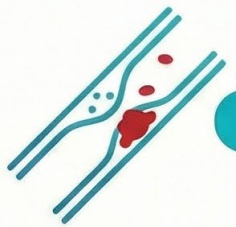
Apixaban for Cancer-Associated Blood Clots: Finding the Right Balance

Reduced Dose is **Equally Effective for Prevention**

The 2.5 mg dose was proven **noninferior** to the full 5.0 mg dose.

Reduced Dose is **Significantly Safer**

It led to a statistically lower incidence of clinically relevant bleeding complications.



Recurrent Blood Clots

2.1%

2.8%
Full Dose
(5.0 mg)

12.1%
Clinically Relevant Bleeding

2.9%
Major Bleeding

15.6%

4.3%
Full Dose (5.0 mg)

ÖZET

- Kanser hastalarında VTE insidansı sağlıklı popülasyona göre yüksek ve son yıllarda daha da artmakta.
- Tedavi seçeneği **DMAH ve DOAKlar**
- GIS tümörlerinde ve kanamalı mesane tümörlerinde **DMAH** tercih edilmeli
- DOAKlardan **Apixaban** daha az kanama yapıyor
- 6 aylık tam doz tedaviden sonra **Apixaban yarı doz (2x2.5)** ile tedaviye devam etmek tam doz kadar etkili.