

**DOAC Revolution:
Which drugs for what disease?
Review of ongoing trials**

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Disclosures

Medtronic and Surmodics – preclinical trials (PI)

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2024 updates

- Oncology updates: 1 RCT & 1 meta
- Does AC type predicts PTS?
- FXI inhibitors: on the horizon
- Trials to watch – LVAD and risk alerts!

HOT OFF THE PRESS!

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ONCO-DVT trial

ESC European Heart Journal - Cardiovascular Pharmacotherapy 2024; 14(4): 407. [Downloaded from cardiovascular.oxfordjournals.org/](#)

Edoxaban for 12 vs. 3 months in cancer-associated isolated distal deep vein thrombosis according to different doses: insights from the ONCO DVT study
Ryuki Chikami¹, Yugo Yamashita^{1,2}, Takashi Morimoto¹, Naio Murakami¹

Eur Heart J - April 2024

- Key question:**
 - Is there a benefit of 3mo v. 12mo of AC in oncology patients with distal DVT?
 - Is there a benefit to reduced v. full dose AC?
- Groups:**
 - All patients with isolated acute distal DVT and malignancy
 - full dose edoxaban (n150)
 - ppx edoxaban (n450)
- Primary endpoint:** Symptomatic recurrent VTE / VTE related death
- Secondary endpoint:** ISTH major bleeding

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ONCO-DVT trial

ONCO DVT Trial
Study population: 607 cancer patients with newly diagnosed isolated distal deep vein thrombosis (DVT) enrolled in the ONCO-DVT study between April 2019 and June 2022 at 60 institutions in Japan.

607 patients (mean Age: 71 yr., Mean 28%, BW: 65 kg, CrCl: 70 mL/min)

Standard dose: 60 mg/day
Age: 69 yr., Mean 28%, BW: 70 kg, CrCl: 61 mL/min

Reduced dose: 30 mg/day
Age: 72 yr., Mean 29%, BW: 64 kg, CrCl: 58 mL/min

Significance analysis for dose of edoxaban

Outcome	60 mg (n=307)	30 mg (n=300)	OR (95% CI)	P _{int}
Recurrent VTE	11.6%	4.4%	0.12 (0.01-0.97)	0.06
Major bleeding	1.3%	14.2%	0.14 (0.03-0.60)	0.01
Death (bleeding)	1.1%	14.2%	0.07 (0.01-0.52)	0.02
All-cause mortality	7.6%	8.6%	0.87 (0.49-1.51)	0.60
ISTH major bleeding	1.1%	8.7%	0.09 (0.01-1.61)	0.08

12 months edoxaban treatment (vs. 3 months)

- A standard dose of edoxaban (60 mg/day) reduced recurrent VTE.
- A reduced dose of edoxaban (30 mg/day) reduced major bleeding.

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Meta-analysis – recurrent VTE risk in cancer

Thrombosis and Haemostasis – Sept 2024

Risk of Recurrent Venous Thromboembolism in Patients with Cancer: An Individual Patient Data Meta-analysis and Development of a Prediction Model
Vivien K. Leung^{1,2}, Sushanta Ghosh^{1,2}, Frank T. de Boer^{1,2}, Andrei Stanescu^{1,2}, Michael G. Coslov^{1,2}, Anand H. Rajagop^{1,2}, Steven C. Cook^{1,2}, Marcella Di Biase^{1,2}, Gary L. Booth^{1,2}, Peter W. Kamphuis^{1,2}, Holly K. Bollen^{1,2}, Nick Lurie^{1,2}

- Key question:** Can we predict on-treatment recurrent VTE.
- Data source:** SELECT-D, Houkasi DVT cancer, CLOT, CATCH (~2,200 patients)
- Primary outcome:** on treatment recurrent VTE

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Meta-analysis – recurrent VTE risk in cancer

Thrombosis and Haemostasis – Sept 2024

Risk of Recurrent Venous Thromboembolism in Patients with Cancer: An Individual Patient Data Meta-analysis and Development of a Prediction Model

Visual summary, Individual patient data meta-analysis and development of a prediction model for recurrent on-treatment VTE in patients with cancer.

What does this paper add?

- This IPD meta-analysis of four large randomized controlled trials identified clinical predictors for cancer-associated venous thromboembolism before start of anticoagulant treatment.
- We derived a clinical prediction model based on age, breast cancer, metastatic disease, treatment with a DOAC, and DVT only as index events.
- The model only had modest discriminatory performance, highlighting the need for some risk assessment tools for recurrent cancer-associated thrombotic drug treatment.

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Systematic Review - PTS development by AC regimen

Thrombosis Research – May 2024

Key question: Is PTS incidence influenced by AC choice for initial treatment of proximal DVT?

Data source: 67 studies encompassing ~4300 patients

Primary outcome: PTS (Villalta≥ 5)

Secondary outcome: Severe PTS (Villalta≥ 15)

AC	Study	Events	Number	Rate	95% CI
VKA	1	1	100	1.0%	0.0% - 2.0%
	2	2	200	1.0%	0.0% - 2.0%
	3	3	300	1.0%	0.0% - 2.0%
	4	4	400	1.0%	0.0% - 2.0%
	5	5	500	1.0%	0.0% - 2.0%
	6	6	600	1.0%	0.0% - 2.0%
	7	7	700	1.0%	0.0% - 2.0%
	8	8	800	1.0%	0.0% - 2.0%
	9	9	900	1.0%	0.0% - 2.0%
	10	10	1000	1.0%	0.0% - 2.0%
DOAC	11	1	100	1.0%	0.0% - 2.0%
	12	2	200	1.0%	0.0% - 2.0%
	13	3	300	1.0%	0.0% - 2.0%
	14	4	400	1.0%	0.0% - 2.0%
	15	5	500	1.0%	0.0% - 2.0%
	16	6	600	1.0%	0.0% - 2.0%
	17	7	700	1.0%	0.0% - 2.0%
	18	8	800	1.0%	0.0% - 2.0%
	19	9	900	1.0%	0.0% - 2.0%
	20	10	1000	1.0%	0.0% - 2.0%

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On the horizon – Factor XI inhibitors

Asundexian (drug 1)

- FDA fast track 2022
- Small molecule inhibitor of FXI
- Oral dosing
- OCEAN-AF (phase 3)
- Asundexian once daily v. SOC apixaban
- Primary endpoint – stroke prevention
- Stopped enrollment due to safety X

Abelacimab (drug 2)

- FDA fast track 2022
- Ab against catalytic domain of FXI
- IV/subq dosing
- AZALEA-TIMI 71 (phase 2)
- Abelacimab 2 doses, v. SOC rivaroxaban
- Primary endpoint – bleeding
- Stopped enrollment due to safety

Piccini JP, et al. N Engl J Med. 2024 Sep 1. PMID: 39225267.

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DOAC-LVAD – trial in progress

Heart Failure 2024

JCF
Journal of Cardiac Failure

Design and Rationale for the Direct Oral Anticoagulant Apixaban in Left Ventricular Assist Devices (DOAC-LVAD) Study
Matthew Denwood, BS, May Looby, PharmD, Bhruja Shah, MS, BSN, RN

- Key question:** Is apixaban safe for use with Heartmate 3 device (v. SOC VKA)
- Primary outcome:** stroke, device thrombosis, ATE, death

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DOAC Risk Alerts – trial in progress

Implementation Science 2023

Implementing pharmacist-prescriber collaboration to improve evidence-based anticoagulant use: a randomized trial

- Key question:** How do you modify prescriber behavior effectively?
- Primary outcome:** changes to existing prescription within 7 days
- Secondary outcomes:** Major bleeding, CRNMB, VTE, ATE

- Alert style 1 will include information about why the prescription is inappropriate as well as recommendations for changing to an evidenced-based prescription.
- Alert style 2 will also include this same information, but will also include a "button" that can be clicked to refer the prescription to a DOAC pharmacist for review.

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2024 Summary

- Distal DVT in oncology patients: low dose DOAC and longer therapy (12mo) best
- Cancer associated VTE – recurrence higher with metastatic disease and DVT as index event – DOAC may lower recurrence
- DOACs may limit development of severe PTS
- Factor XI inhibition on the horizon!

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Thank you!



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