MICHIGAN MEDICINE
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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) 10, 422–431 https://doi.org/10.1093/ehjcvp/pvae028 ORIGINAL ARTICLE Thrombosis and antithrombotic therapy

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 Chatani[1], Yugo Yamashita[2,3*], Takeshi Morimoto[4], Nao Muraoka[5],

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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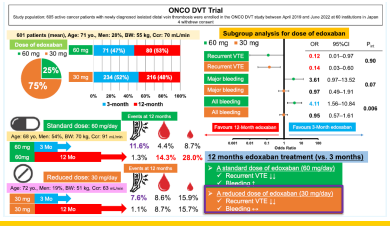
ONCO-DVT trial



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Meta-analysis – recurrent VTE risk in cancer

Thrombosis and Haemostasis – Sept 2024

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

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

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Meta-analysis – recurrent VTE risk in cancer

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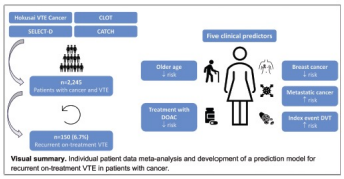

Risk of Recurrent Venous Thromboembolism in Patients with Cancer: An Individual Patient Data Meta-analysis and Development of a Prediction Model

What does this paper add?

- This IPD meta-analysis of four large randomized controlled trials identified clinical predictors for recurrent cancer-associated thrombosis 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 new risk assessment tools for recurrent cancer-associated thrombosis during treatment.

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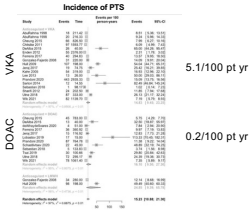
Systematic Review - PTS development by AC regimen

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)



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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

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

Design and Rationale for the Direct Oral Anticoagulant Apixaban in Left Ventricular Assist Devices (DOAC LVAD) Study

Matthew Dimond, BS, Mary Looby, PharmD, Bhruga Shah, MS, BSN-RN,

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DOAC Risk Alerts – trial in progress

Implementation Science 2023

- 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

STUDY PROTOCOL Open Access

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

- 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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