ImmunoScience Academy

Partnering for Education & Optimizing Treatment in ImmunoScience

Treatment of Cancer-Associated Thrombosis

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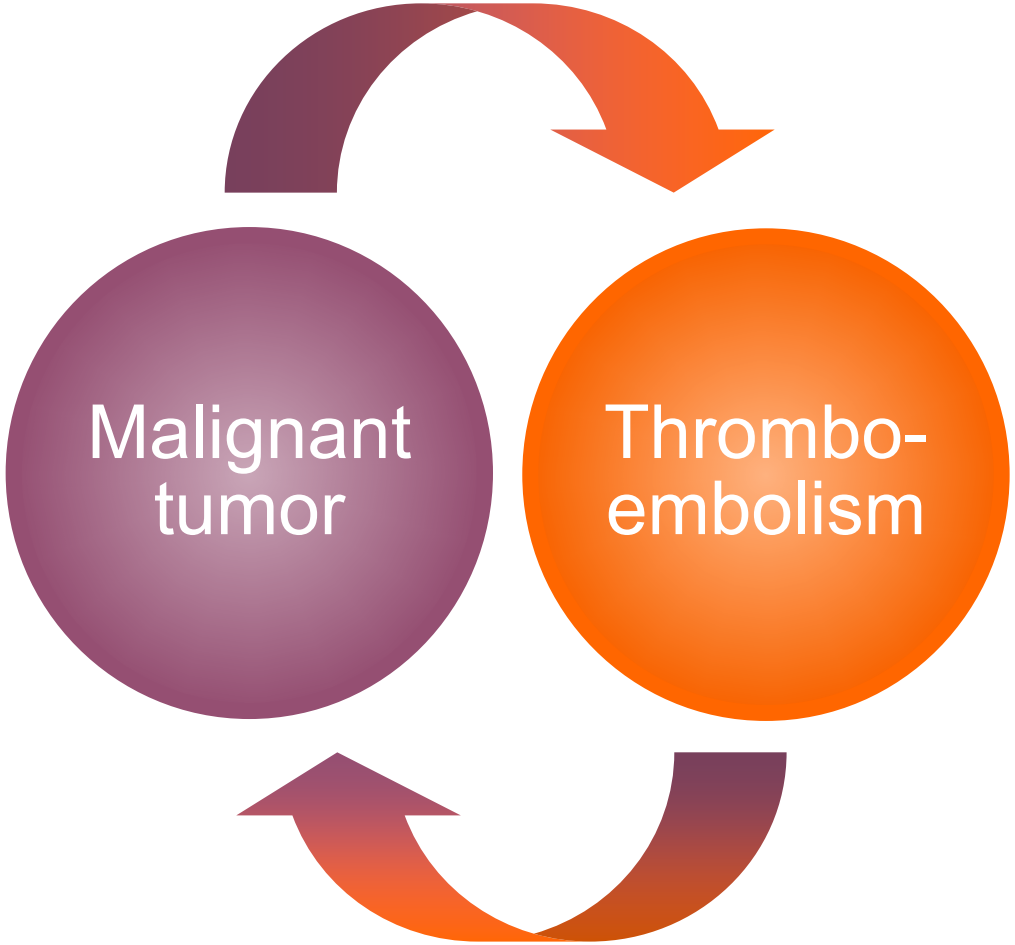
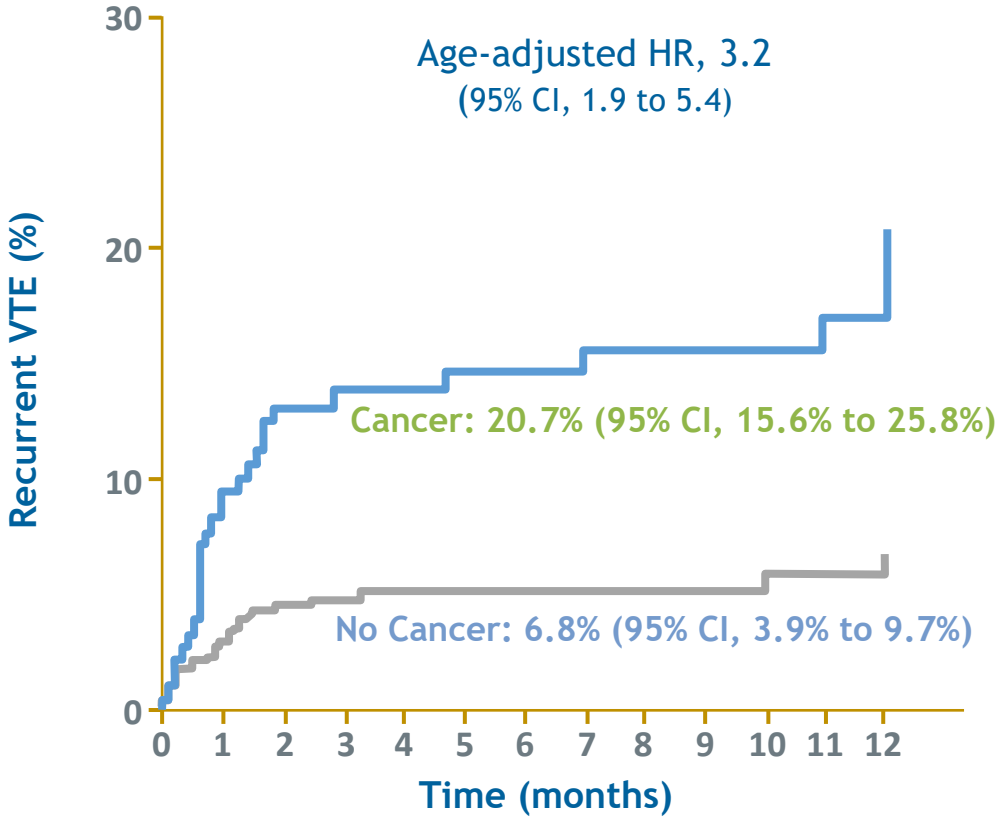
Thrombosis and Cancer

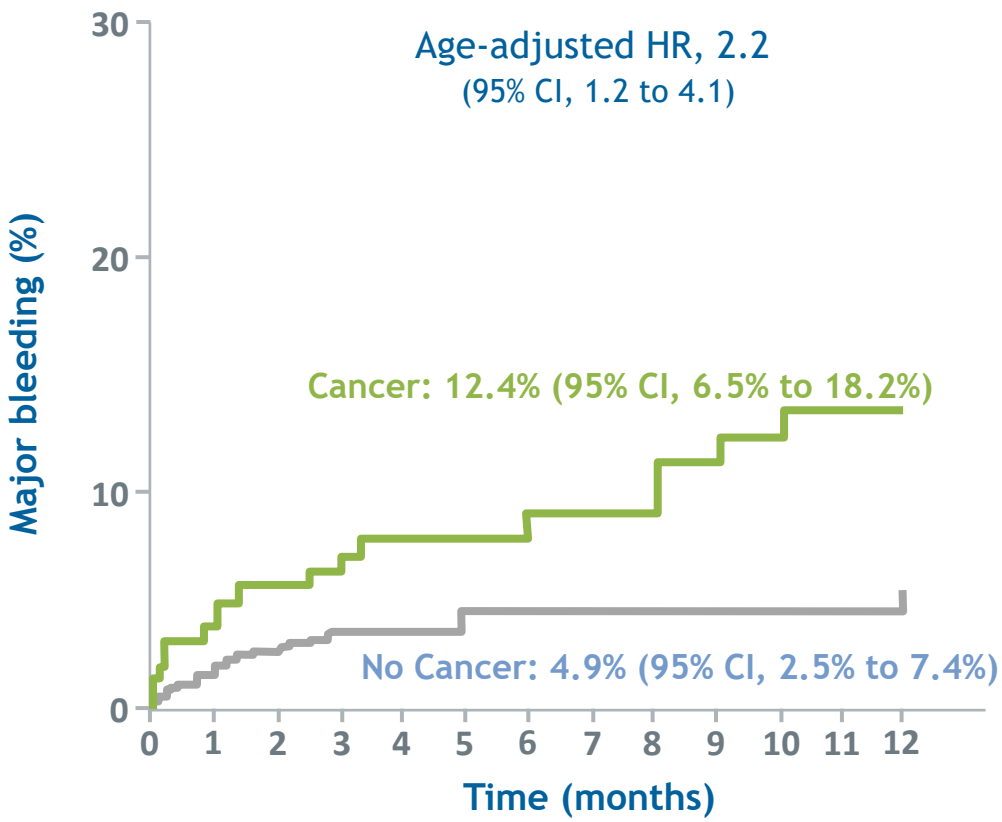


Cancer-Associated Thrombosis: challenges

- How to treat?
- How to diagnose?
- Impact on the cancer treatment and prognosis
- When to prevent?
- Challenging clinical scenarios

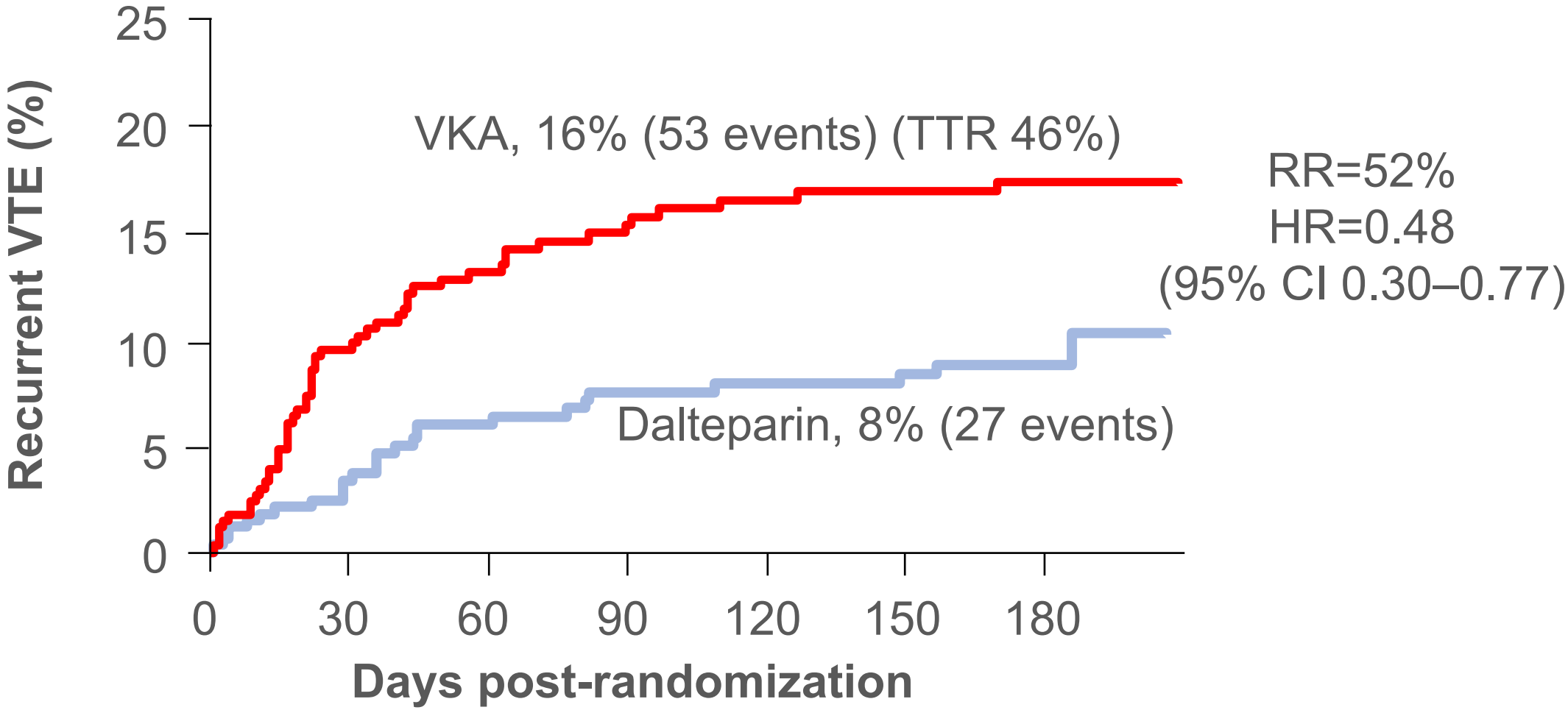
Recurrent VTE and bleeding during anticoagulation in patients with cancer





Prandoni P et al. *Blood*. 2002;100(10):3484-3488.

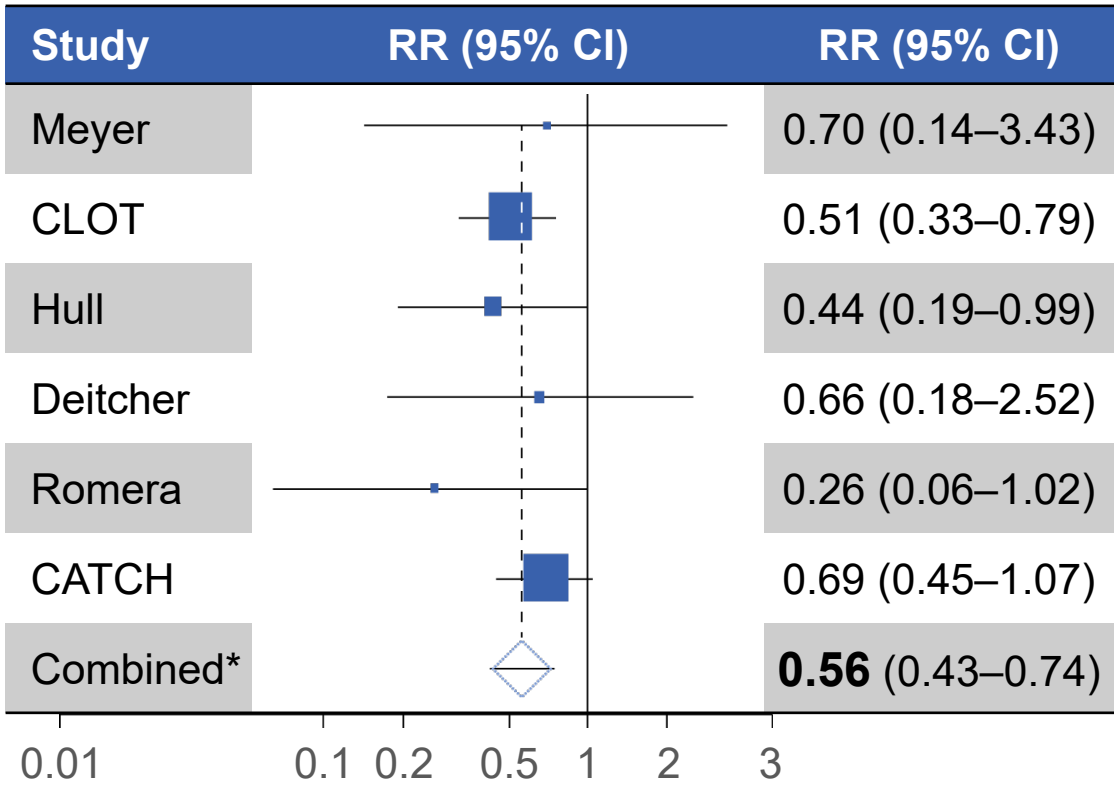
LMWH: the standard of care
CLOT-study: A Landmark



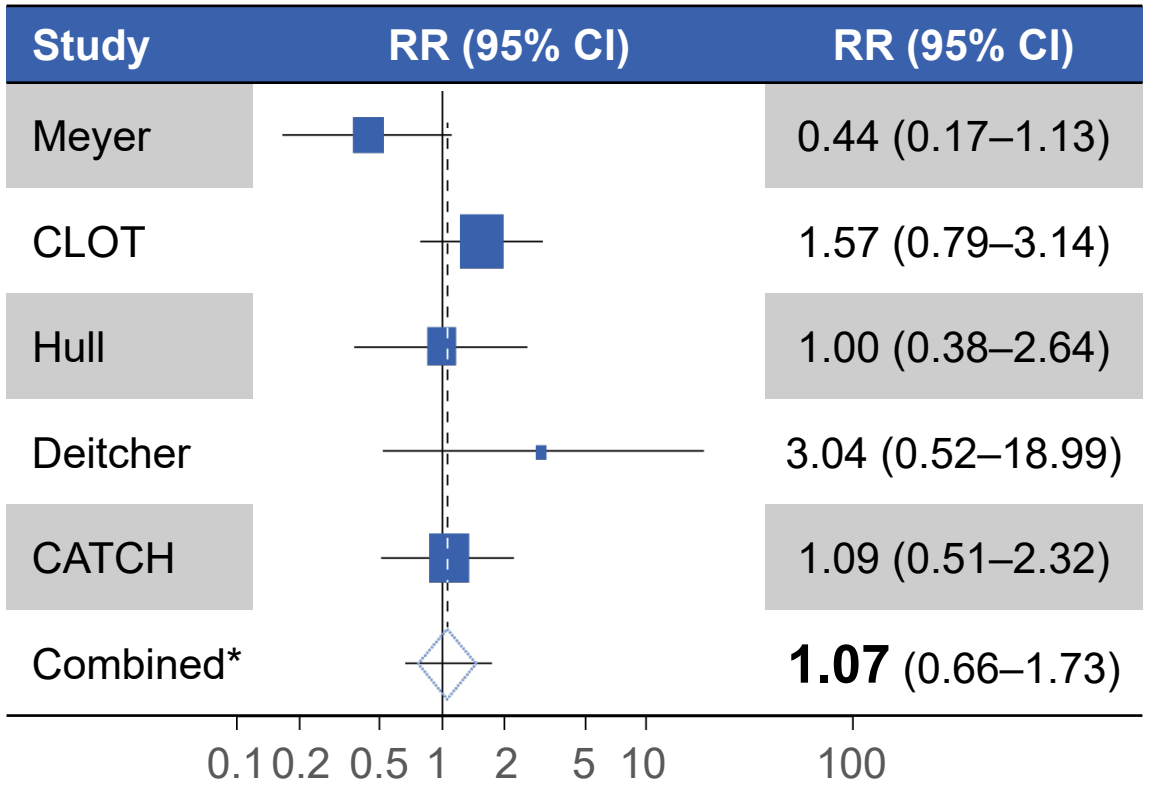
Lee AY et al. *N Engl J Med*. 2003;349(2):146-153.

LMWH versus VKA for Cancer-Associated Thrombosis

Recurrent VTE



Major bleeding events



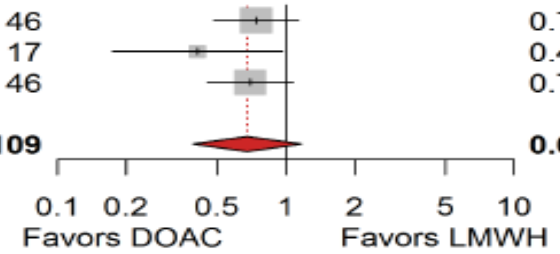
Carrier M et al. *Expert Rev Hematol*. 2017;10(1):15-22.

Main outcomes at 6 months from Hokusai-VTE Cancer, SELECT-D and Caravaggio

Recurrent VTE

Study	DOAC agent	DOAC Patients	DOAC Event	LMWH Patients	LMWH Event	Risk Ratio	RR	95%-CI	Weight
Hokusai VTE Cancer	edoxaban	522	34	524	46		0.74	[0.48; 1.14]	45.4%
SELECT-D	rivaroxaban	203	7	203	17		0.41	[0.17; 0.97]	11.2%
Caravaggio	apixaban	576	32	579	46		0.70	[0.45; 1.08]	43.4%
Random effects model		**1301**	**73**	**1306**	**109**		**0.68**	**[0.39; 1.17]**	**100.0%**

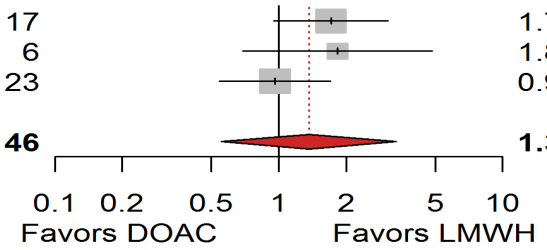
Heterogeneity: $I^2 = 0\%$, $\tau^2 < 0.0001$, $p = 0.48$



Major bleeding

Study	DOAC agent	DOAC Patients	DOAC Event	LMWH Patients	LMWH Event	Risk Ratio	RR	95%-CI	Weight
Hokusai VTE Cancer	edoxaban	522	29	524	17		1.71	[0.95; 3.08]	40.3%
SELECT-D	rivaroxaban	203	11	203	6		1.83	[0.69; 4.86]	18.0%
Caravaggio	apixaban	576	22	579	23		0.96	[0.54; 1.71]	41.7%
Random effects model		**1301**	**62**	**1306**	**46**		**1.36**	**[0.55; 3.35]**	**100.0%**

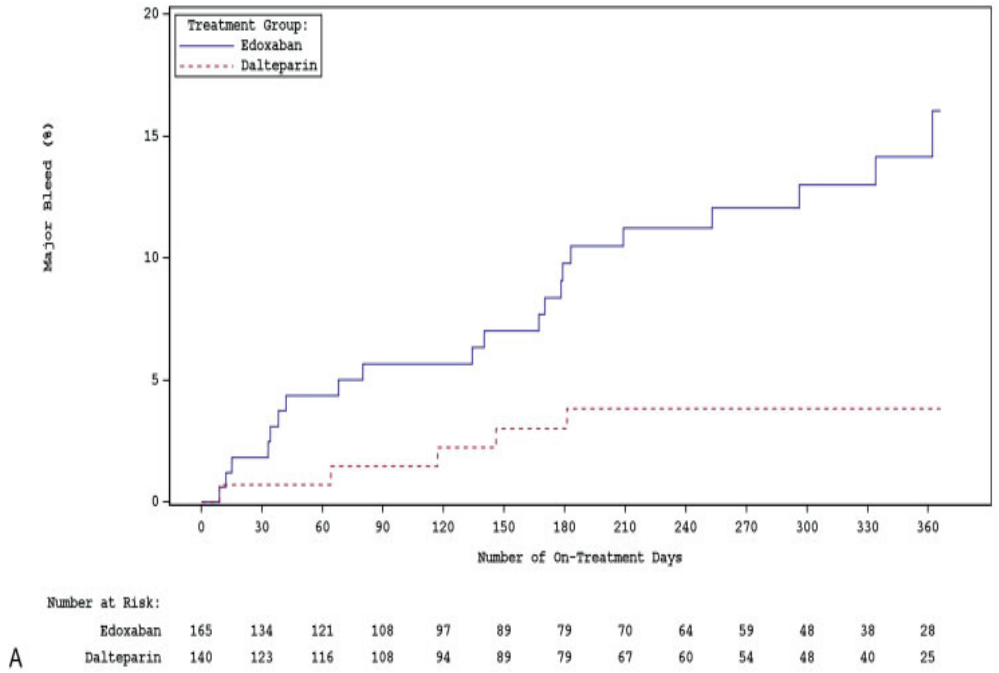
Heterogeneity: $I^2 = 15\%$, $\tau^2 = 0.0379$, $p = 0.31$



Mulder FI et al. *Blood*. 2020;136(12):1433-1441.

Major bleeding events in patients with Cancer-Associated VTE

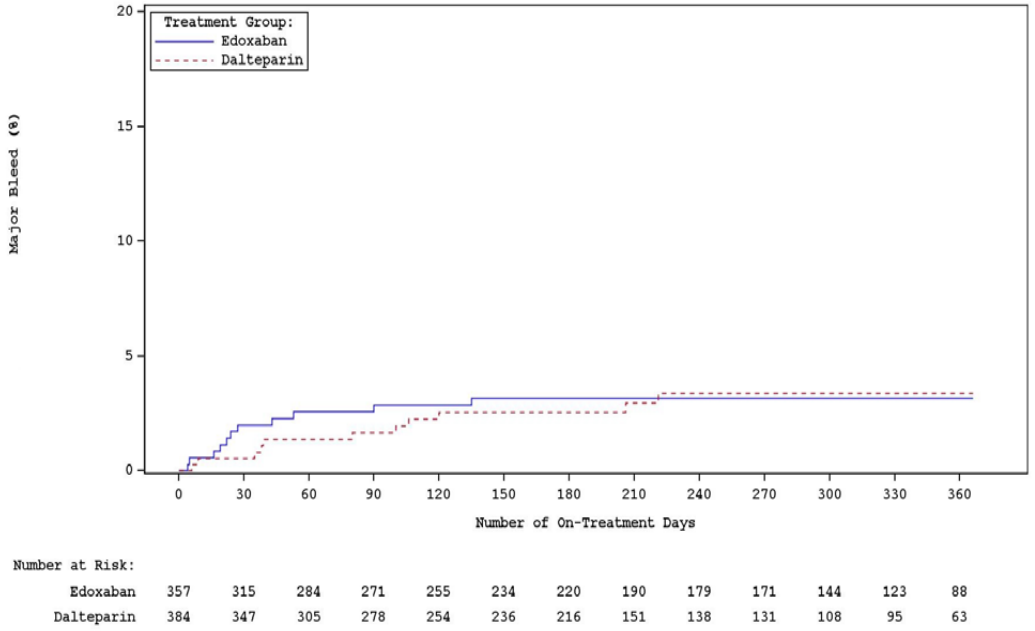
GI cancers



A

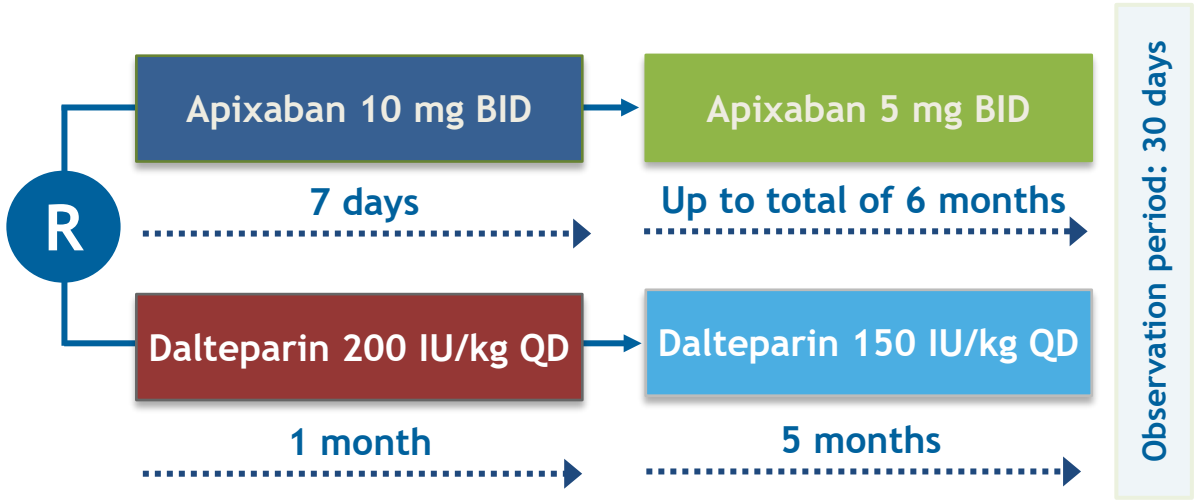
HR 4.0 (95% CI 1.5–10.6)
***p*=0.005**

Non-GI cancers



Kraaijpoel N et al. *Thromb Haemost*. 2018;118(8):1439-1449.

Caravaggio: apixaban vs. dalteparin in CAT



Patient Population

- Aged ≥18 years
- Patients newly diagnosed with DVT or PE
- Any type of cancer (other than basal-cell or squamous-cell carcinoma of the skin, primary brain tumor or known intracerebral metastasis and acute leukemia)

Primary Outcome

- recurrent VTE

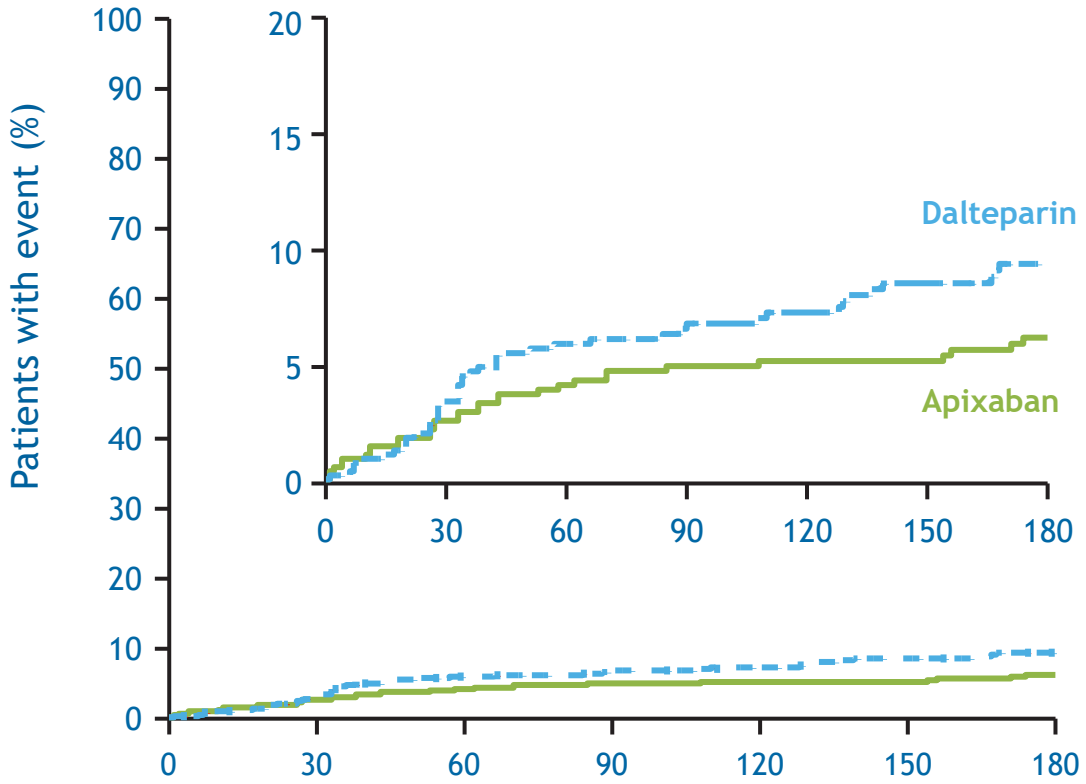
Principal Safety Outcome

- Major bleeding

Agnelli G et al. *N Engl J Med*. 2020;382(17):1599-1607 and supplementary appendix available online.

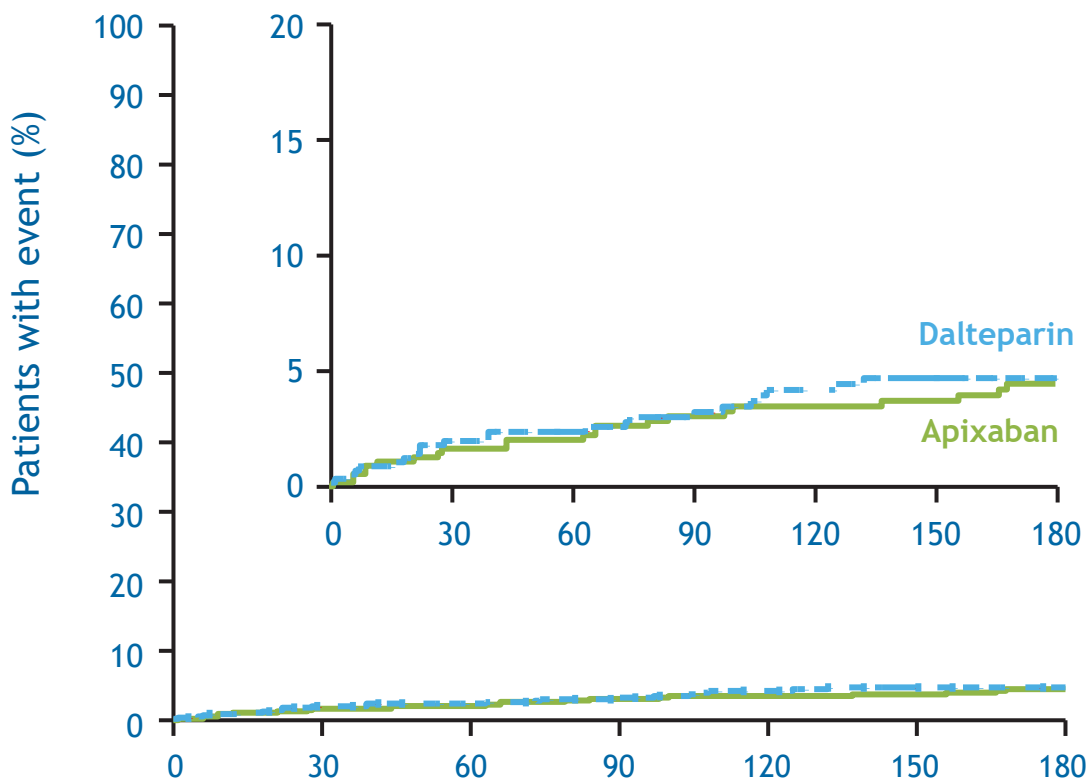
Caravaggio: recurrent VTE and major bleeding

Recurrent Venous Thromboembolism



Number at Risk							
Dalteparin	579	507	462	417	383	352	217
Apixaban	575	522	481	453	424	399	241

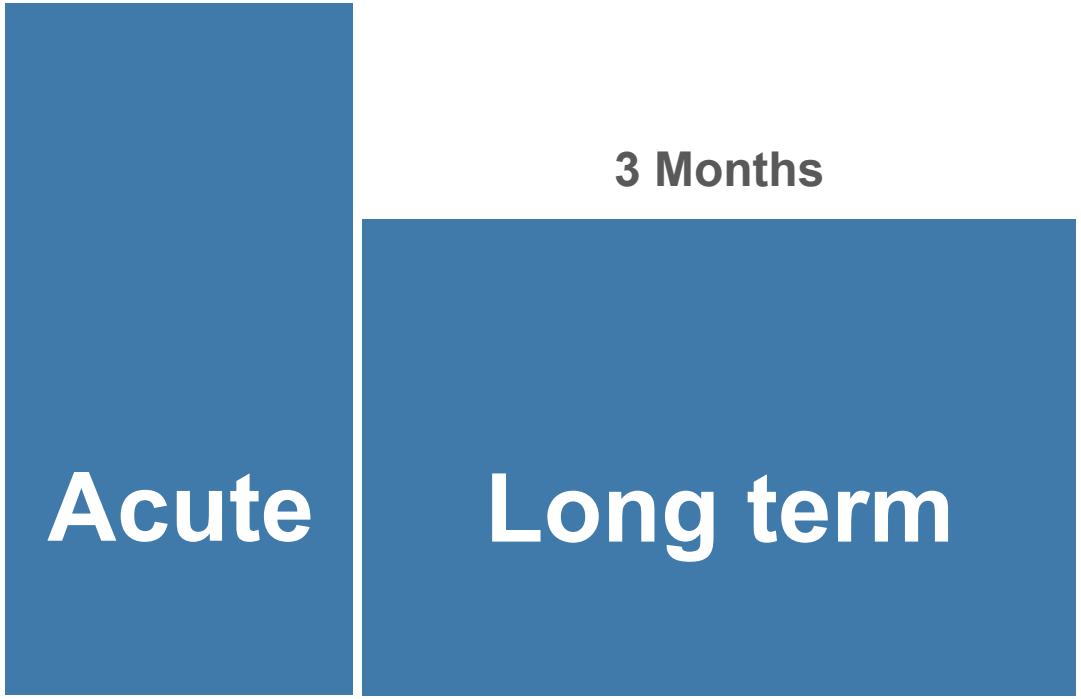
Major Bleeding



Number at Risk							
Dalteparin	579	510	473	430	387	355	222
Apixaban	575	527	490	458	427	402	238

Agnelli G et al. *N Engl J Med*. 2020;382(17):1599-1607

Which patients should receive long-term anticoagulation?

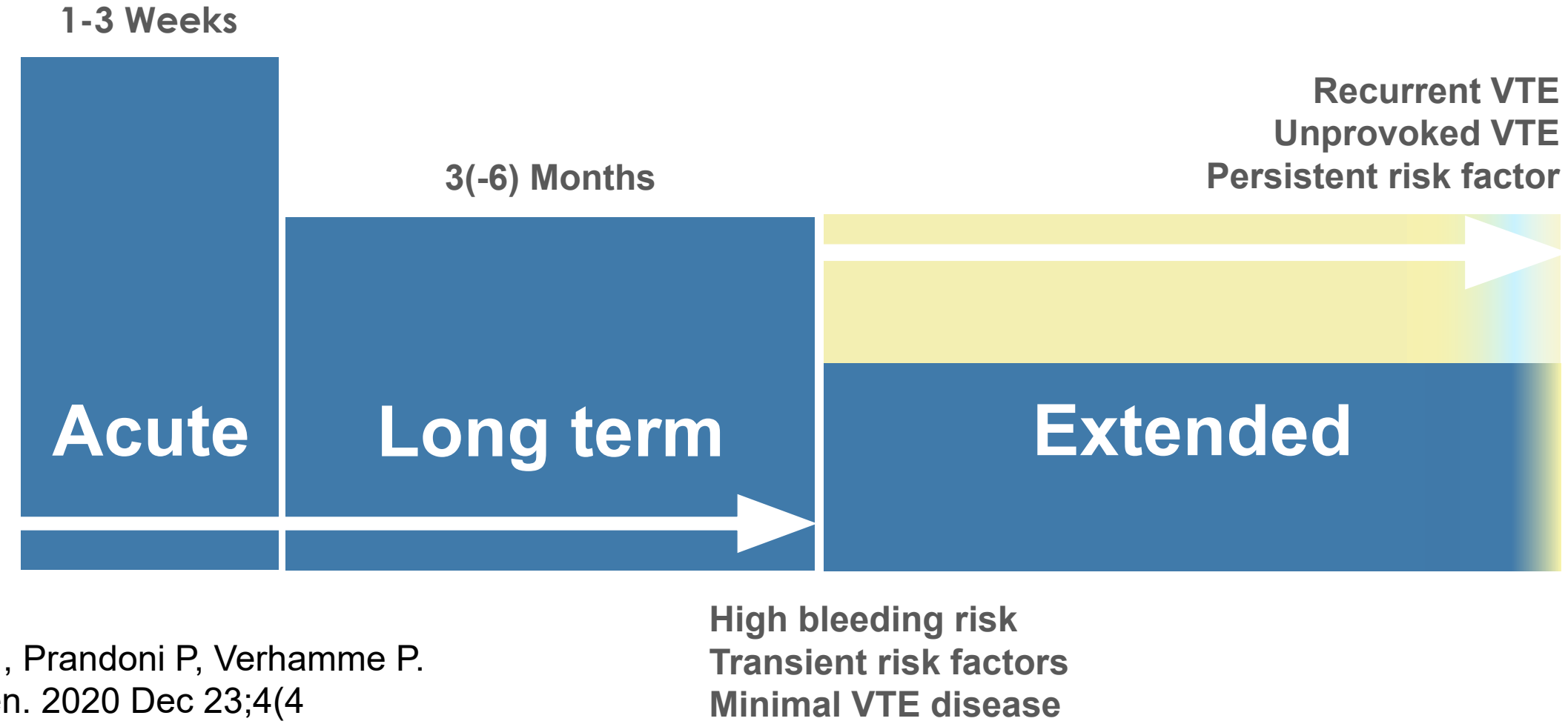


Treatment

?

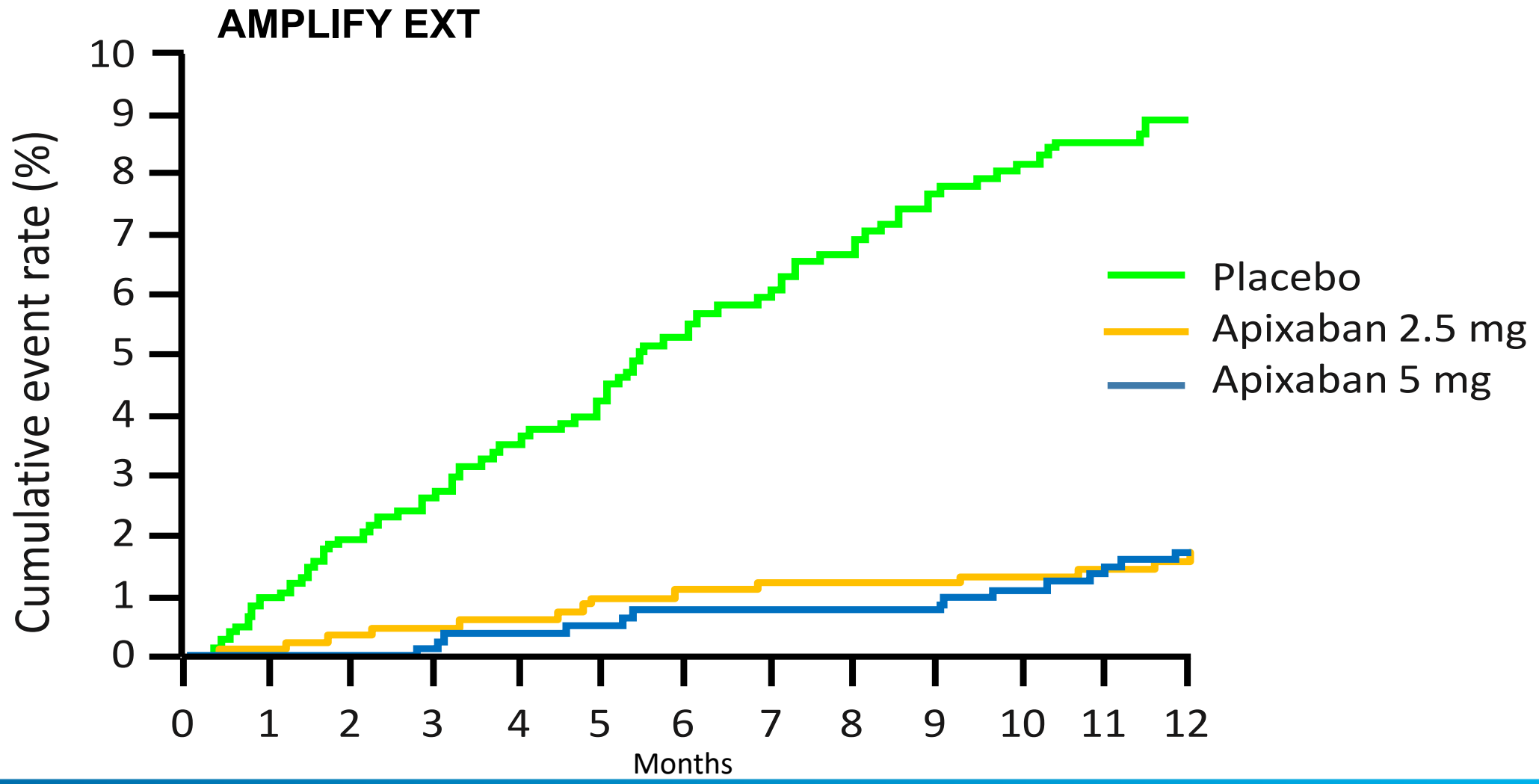
Prevention

Duration of anticoagulation for VTE



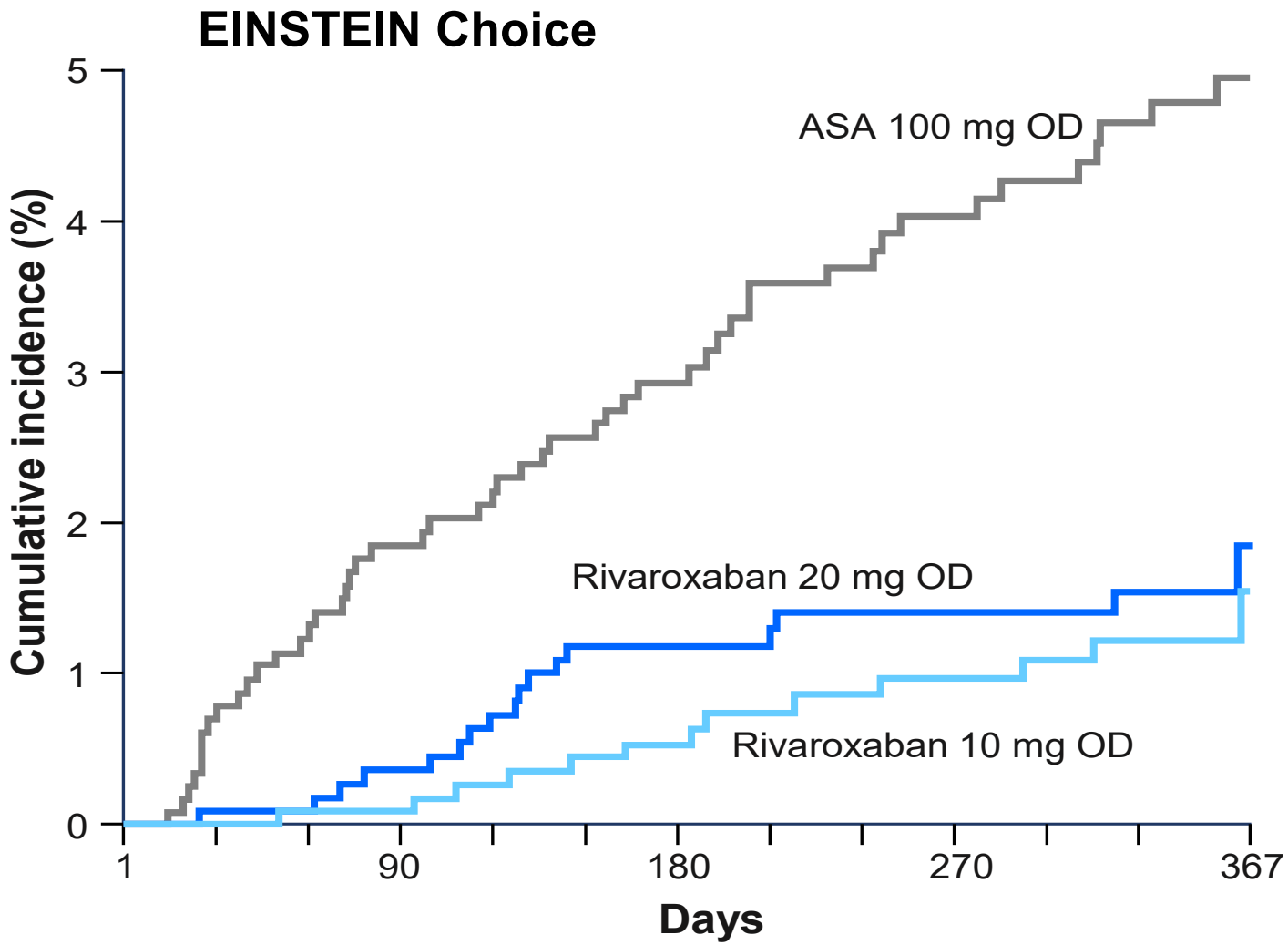
Weitz JI, Prandoni P, Verhamme P.
TH Open. 2020 Dec 23;4(4

Reduced dose NOAC for long-term prevention?



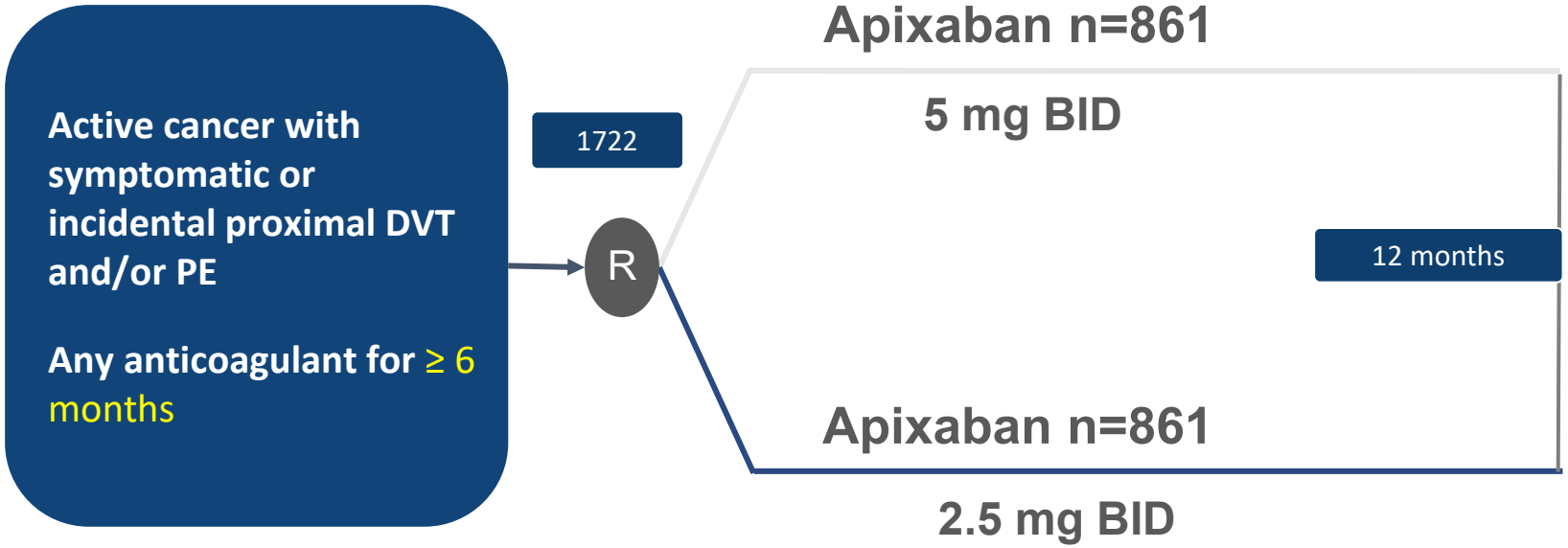
Agnelli G et al. *N Engl J Med*. 2013;368(8):699-708.

Reduced dose NOAC for long-term prevention?



Weitz JI et al. *N Engl J Med*. 2017;376(13):1211-1222.

APICAT Study

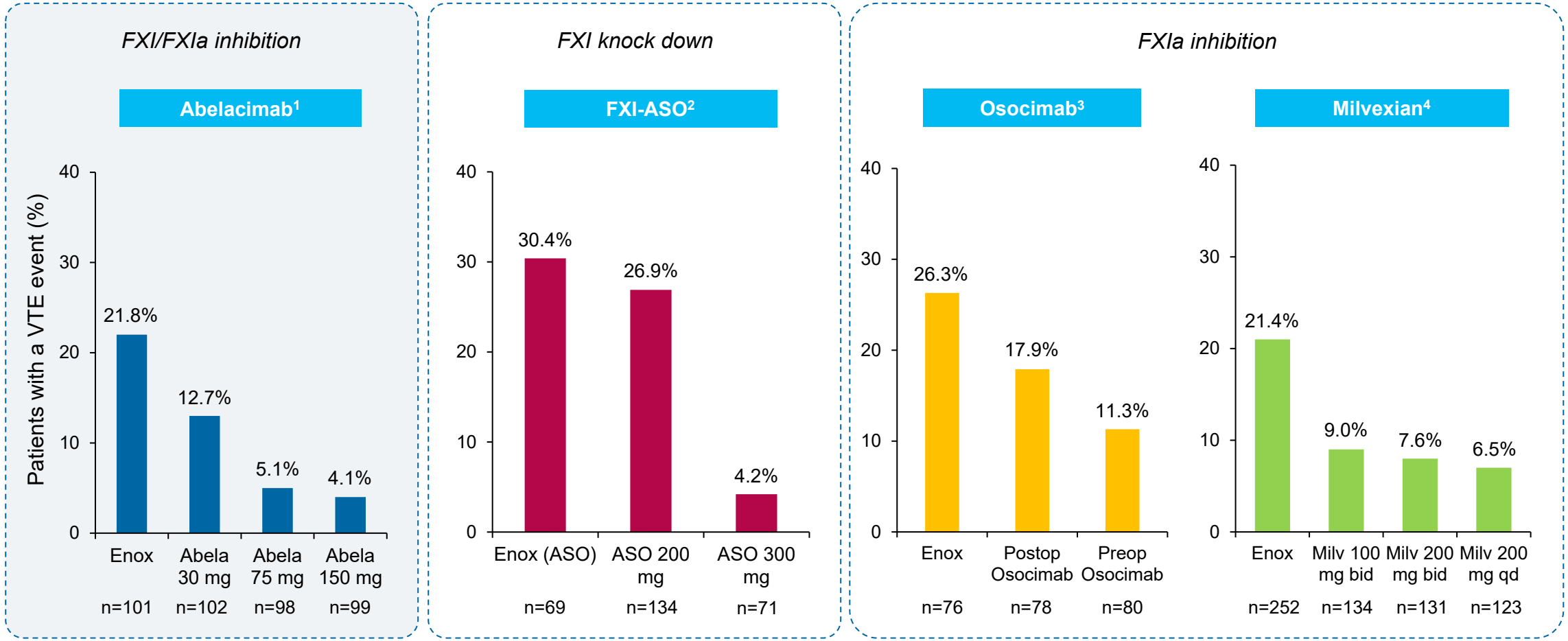


* **NCT03692065**

ClinicalTrials.gov. Accessed Oct 2022. https://clinicaltrials.gov/ct2/show/NCT03692065

Demonstration of antithrombotic ‘proof-of-concept’ with FXI inhibitors

Cross-study comparison of FXI agents after major orthopedic surgery



There are no head-to-head randomised clinical trials comparing the products mentioned above. Comparisons cannot be made between individual products based on these data.

*p<0.05 for superiority

1. Verhamme P et al. *N Engl J Med*. 2021;385(7):609-617; 2. Büller HR et al. *N Engl J Med*. 2015;372(3):232-240; 3. Weitz JI et al. *JAMA*. 2020;323(2):130-139; 4. Weitz JI et al. *N Engl J Med*. 2021;385(23):2161-2172.

Managing daily challenges

- Low platelets
- Renal function
- Extremes of body weight
- Drug-drug interactions

Optimal dosing?

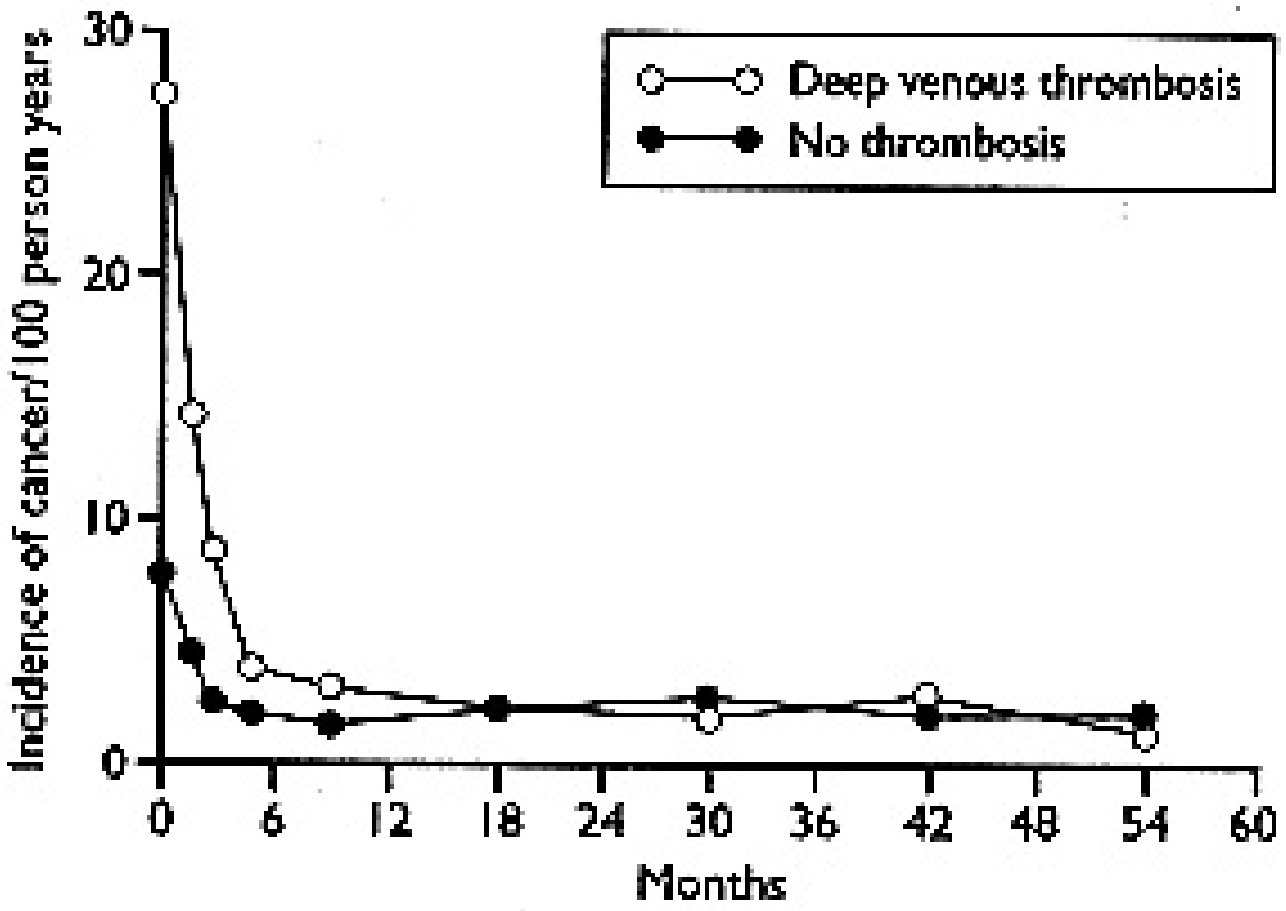
- Recurrent TE
- Incidental VTE
- Port-a-cath & UE DVT
- Arterial TE
- Management post-bleeding

What is important for patients?

1. No interference with cancer treatment	39%
2. Efficacy / recurrent VTE	24%
3. Major bleeding	19%
4. Route of Administration	13%
5. Monitoring	2%
6. Minor bleeding	2%
7. Frequencency of administration	1%

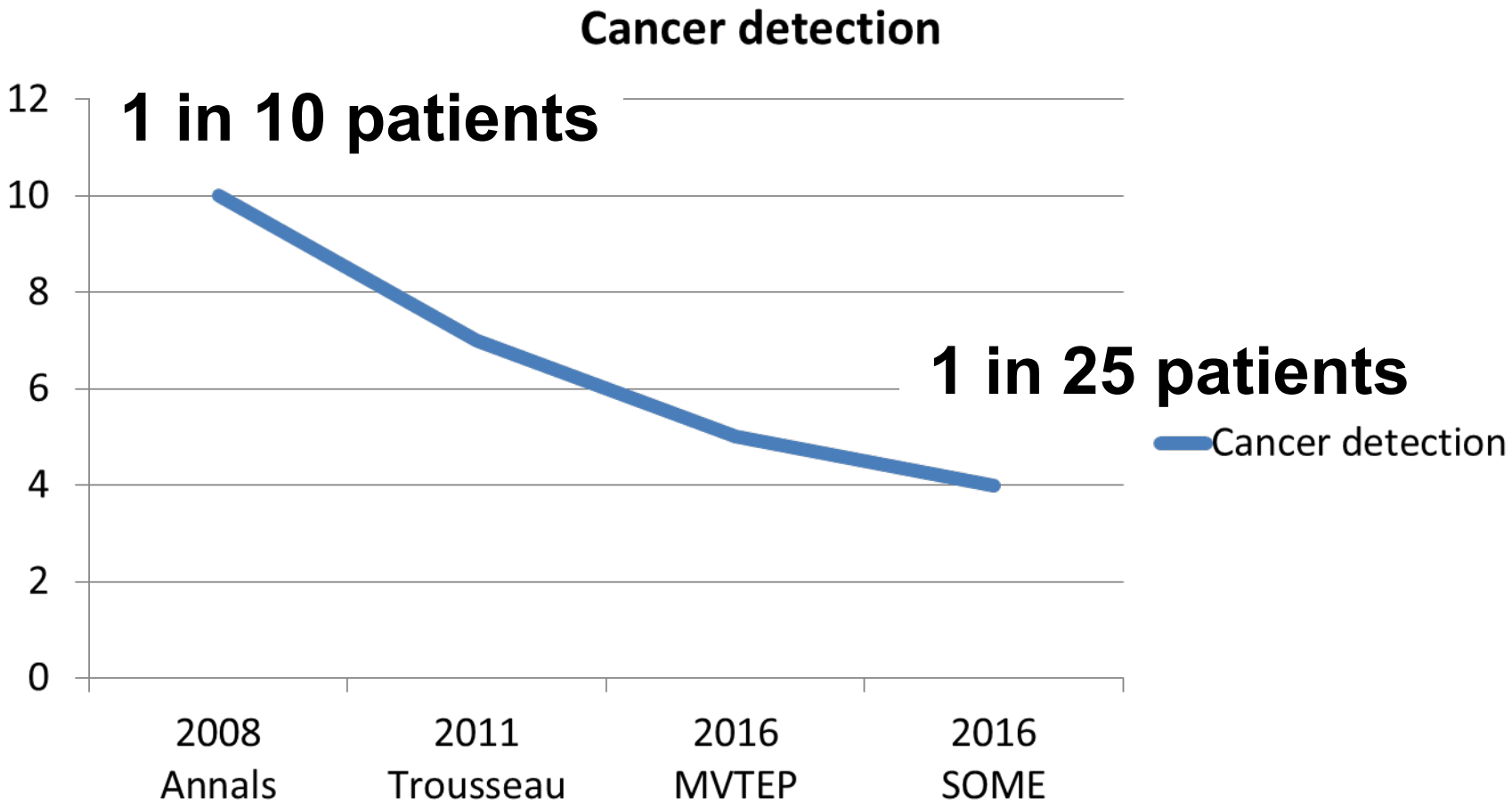
Noble S et al. *Haematologica*. 2015;100(11):1486-1492.

Incidence of cancer in patients with DVT



Nordström M et al. *BMJ*. 1994;308(6933):891-894.

Incidence of occult cancer detection in the different studies



D'Astous J, Carrier M. *J Clin Med.* 2020 Jul 27;9(8):2389.

Occult cancer screening in VTE patients

Why?

- Earlier detection
  - Curable cancer
  - ↑ survival
  - ↓ morbidity

Why not?

- Unnecessary invasive procedures
  - “Incidental findings”
- No impact on outcome
- Anxiety
- Costs

D'Astous J, Carrier M. *J Clin Med.* 2020 Jul 27;9(8):2389.

Limited vs. extensive occult cancer screening strategy

SOMIT

Trousseau

SOME

MTVEP

D'Astous J, Carrier M. *J Clin Med.* 2020 Jul 27;9(8):2389.

Patients with unprovoked VTE should undergo

- Medical history and physical examination
- Basic laboratory investigations
- Chest X-ray
- Age- and gender- specific cancer screening (i.e., cervical, breast, prostate and colon)

Khorana AA et al. *J Thromb Thrombolysis*. 2016;41(1):81-91.

Treatment of CAT

- No ‘One size fits all’ approach
- Patient selection is key:
  - Tumor type
  - Bleeding risk/renal function/thrombus burden…
  - Drug-drug interactions
  - Patient preferences

A review of latest clinical practice guidelines for the management of cancer-associated thrombosis.
Frere C, Wahl C, Rueda-Camino JA, Crichi B, Prata PH, Marjanovic Z, Farge D. Best Pract Res Clin Haematol. 2022