

Studie HOKUSAI-VTE CANCER

léčba žilního tromboembolismu v souvislosti s karcinomem



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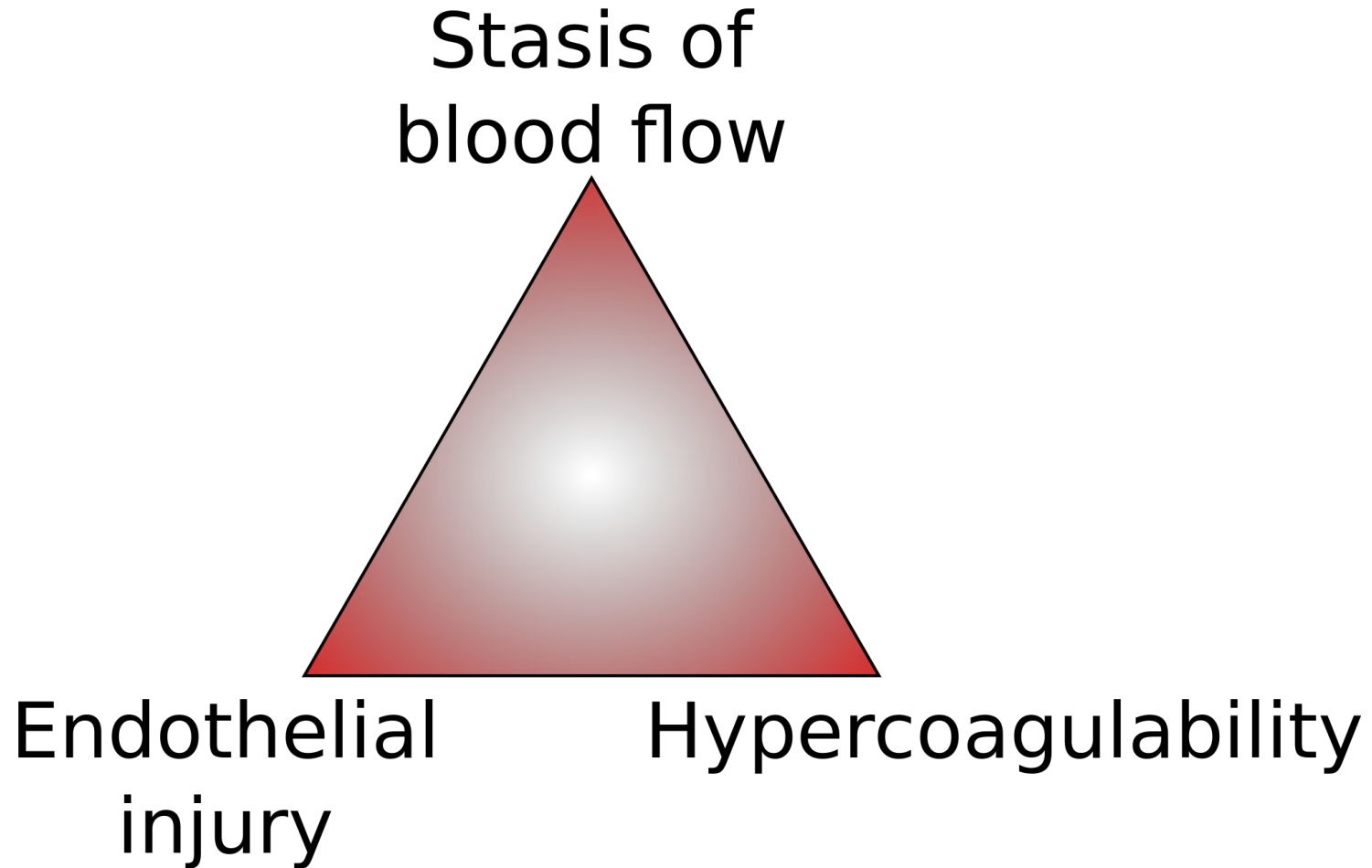
Nádor a tromboembolická nemoc

- Incidence TEN je 1:1000
- 20-30% nemocných s nádorem prodělá TEN
- Nádor zvyšuje riziko TEN 4-7 x
- Riziko krvácení u nemocných s nádorem je 8-10% ročně
- Riziko recidivy je 20% ročně

Rudolf Virchow 1821 - 1902



Virchow triad 1856



Armand Trousseau (1801-1867)



Léčba TEN u nemocného s nádorem

Heparin

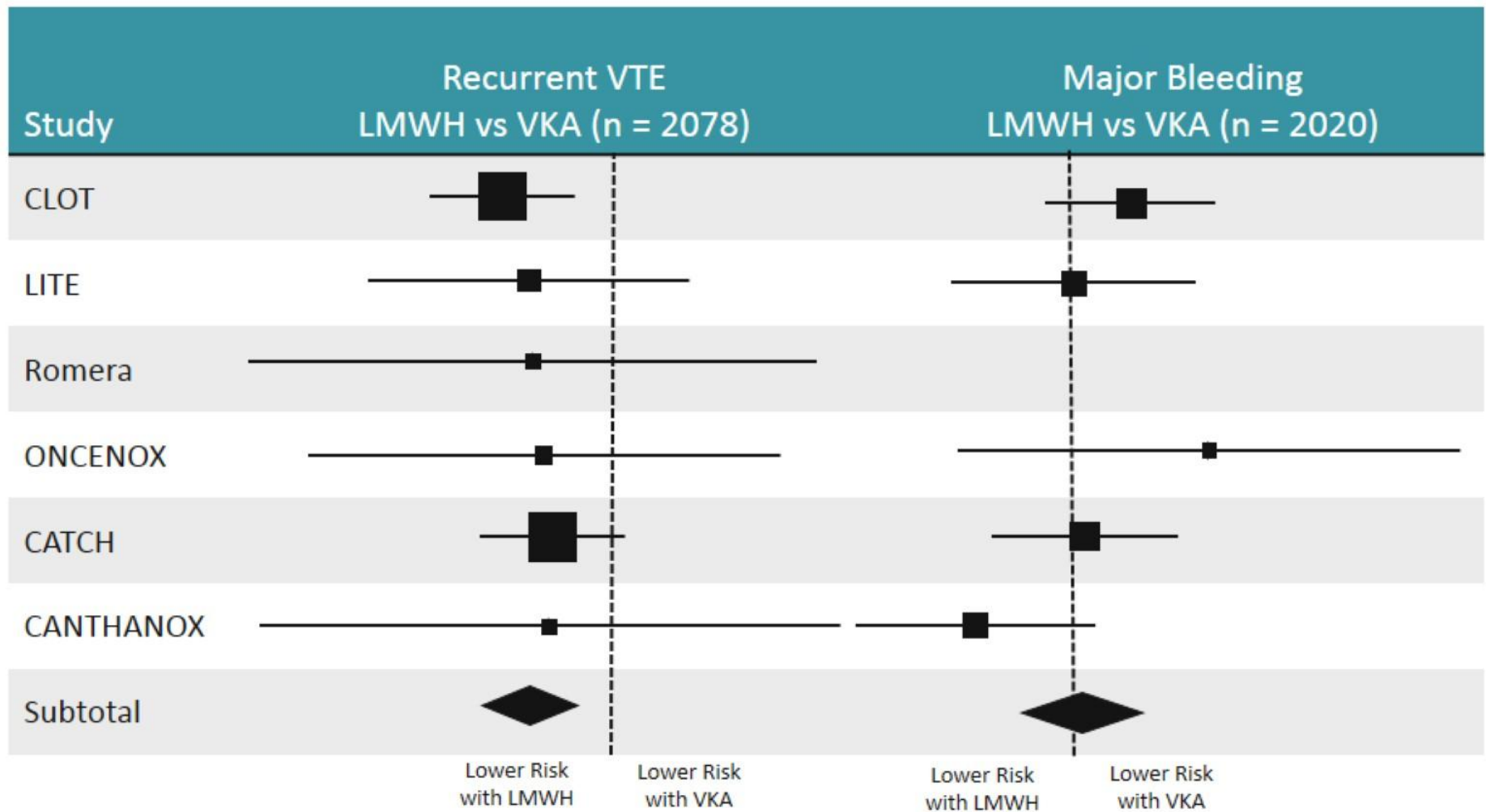


Warfarin



LMWH

LMWH vs VKA in Patients With Cancer: Efficacy (Recurrent VTE) and Safety (Major Bleeding)



$I^2 = 0.0\%$; $P = .963$; $I^2 = 23.1\%$; $P = .267$

Posch F, et al. *Thromb Res.* 2015;136:582-589.

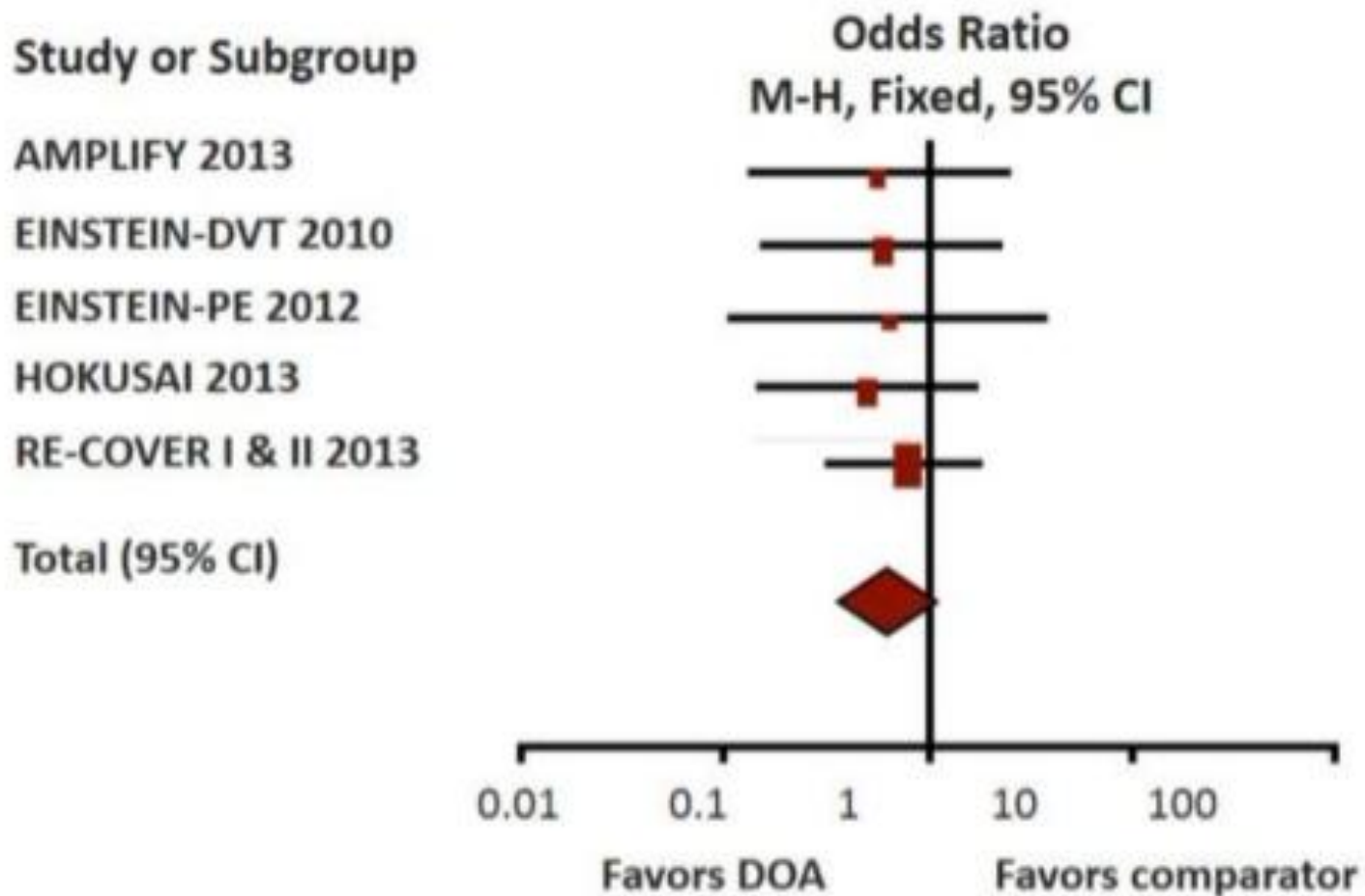
Table 2. Guidelines for Managing VTE in Cancer Patients

Recommendation	NCCN (2014)	ASCO (2015)	ACCP (2015)
Initial therapy	LMWH preferred	LMWH recommended	LMWH recommended
Chronic therapy	LMWH preferred over warfarin for 1st 6 mo	LMWH preferred for ≥ 6 mo	LMWH preferred Extended therapy >3 mo recommended. In patients not treated with LMWH, VKA suggested over rivaroxaban or dabigatran
Chronic outpatient treatment	Novel oral anticoagulants not currently recommended for VTE thromboprophylaxis or treatment owing to insufficient clinical data in cancer patients	Novel oral anticoagulants not currently recommended for patients with cancer and VTE owing to limited data in cancer patients	LMWH and VKA recommended over rivaroxaban or dabigatran

ACCP: American College of Chest Physicians; ASCO: American Society of Clinical Oncology; LMWH: low-molecular-weight heparin; NCCN: National Cancer Comprehensive Network; VKA: vitamin K antagonist; VTE: venous thromboembolism. Source: References 15, 19, 20.

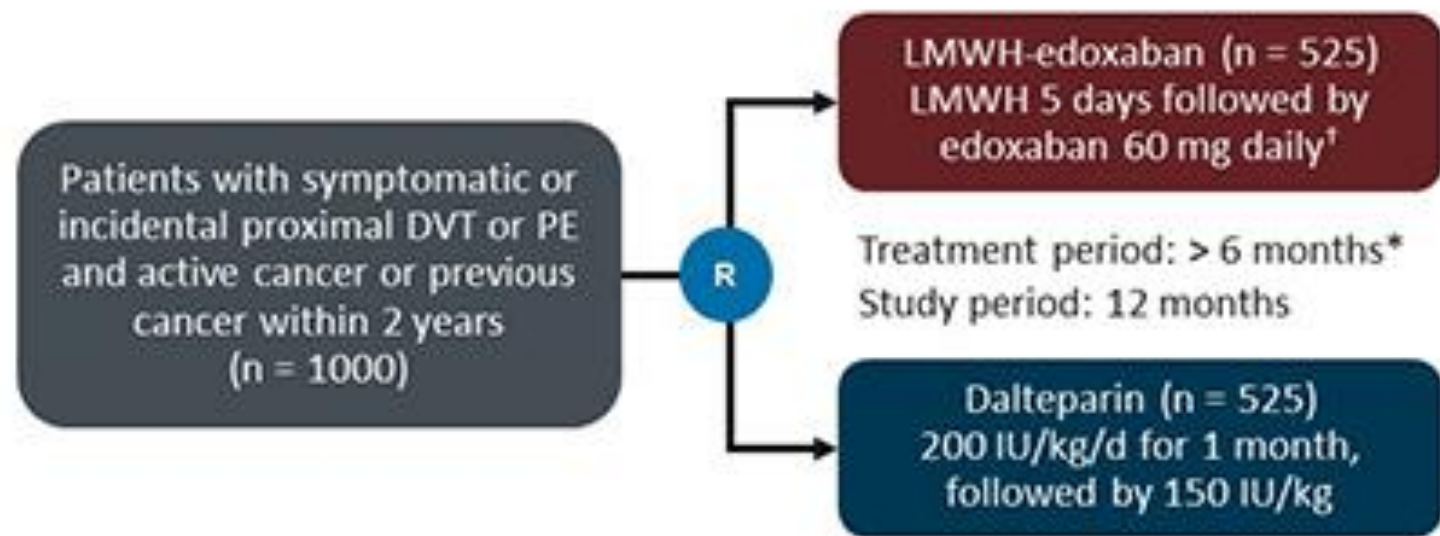
Patients With Active Cancer From Phase 3 VTE Rx Studies

Recurrent VTE



Hokusai-VTE Cancer: Study Design

- Prospective, randomized, open-label, multicenter noninferiority study comparing dalteparin with LMWH-edoxaban for 12 months



- Primary outcome: Composite of recurrent VTE (symptomatic VTE, incidental VTE, or death due to PE) or major bleeding

*Intention is to treat patients for 12 months with the study treatment, but continuation of anticoagulation beyond 6 months will be based on the risk-benefit assessment of the treating physician and/or the patient preference; [†]dose adjustment to 30 mg/d in patients with body weight ≤ 60 kg, creatinine clearance between 30 and 50 mL/min, or concomitant use of P-glycoprotein inhibitors.

Baskob GE, et al. *N Engl J Med*. 2017 [Epub ahead of print]; Van Es N, et al. *Thromb Haemost*. 2015;114:1268-1276.

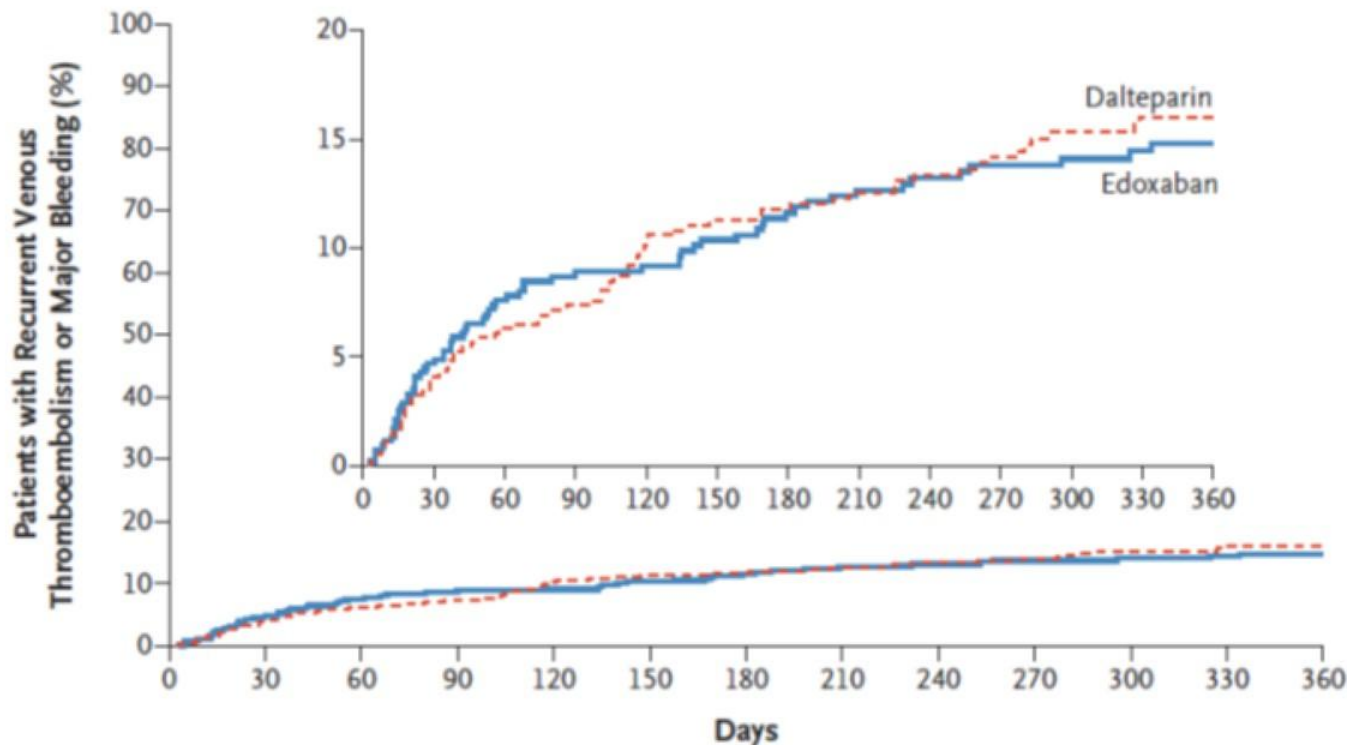
Kacuška Hokusai (葛飾北斎) (1760-1849)



Výsledky (%)

	edoxaban	dalteparin
Mortalita	39.9	36.6
Fatální krvácení	0	0.4

Hokusai VTE Cancer: Cumulative Event Rate for Primary Endpoint



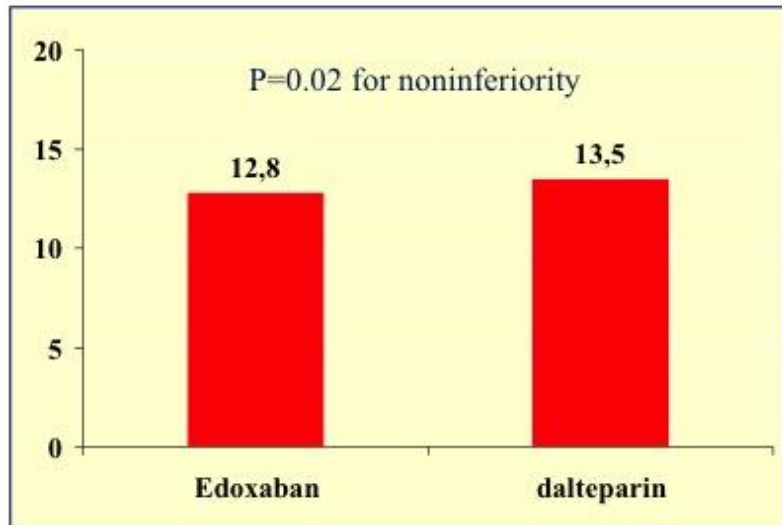
No. at Risk

Edoxaban	522	472	429	407	388	360	345	328	310	295	270	237	161
Dalteparin	524	485	449	420	385	364	352	340	324	313	276	241	171

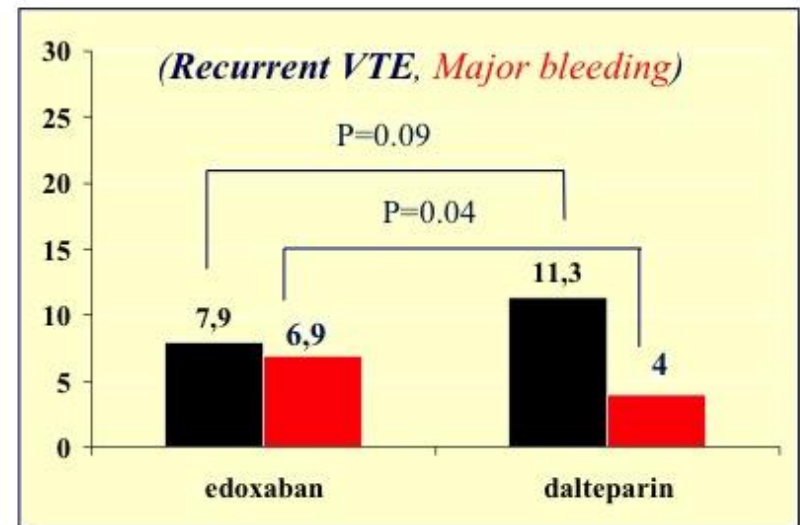
From *N Engl J Med*, Raskob GE, et al., Edoxaban for the Treatment of Cancer-Associated Venous Thromboembolism, [Epub ahead of print]. Copyright © 2017 Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society.

Hokusai VTE Cancer

Primary-outcome events



Secondary-outcome events



Hokusai VTE-Cancer: Types of Major Bleeds Contributing to Primary Outcome

	Edoxaban (n = 522)	Dalteparin (n = 524)
Major bleeding, no. (%)	33 (6.3)	17 (3.2)
Fatal	0	2 (0.4)
Intracranial	2 (0.4)	4 (0.8)
Gastrointestinal	20 (3.8)	6 (1.1)
Upper	17 (3.3)	3 (0.6)
Lower	3 (0.6)	3 (0.6)
Urogenital	5 (1.0)	0
Other	6 (1.1)	7 (1.3)

Zvýšené riziko krvácení

- Nemocný s kolorektálním karcinomem má 3x vyšší riziko krvácení z horní části GIT.

SELECT-D

Study Design

Prospective, randomized, open-label, multicenter, pilot trial
in selected patients with cancer at risk for VTE recurrence
Estimated enrollment: 530 patients

Rivaroxaban
15 mg orally twice daily × 3 weeks
20 mg once daily × 6 months

Dalteparin
200 IU/kg daily subcutaneously × 1 month
150 IU/kg months 2 to 6

Residual vein thrombosis-positive patients

Rivaroxaban
20 mg once daily

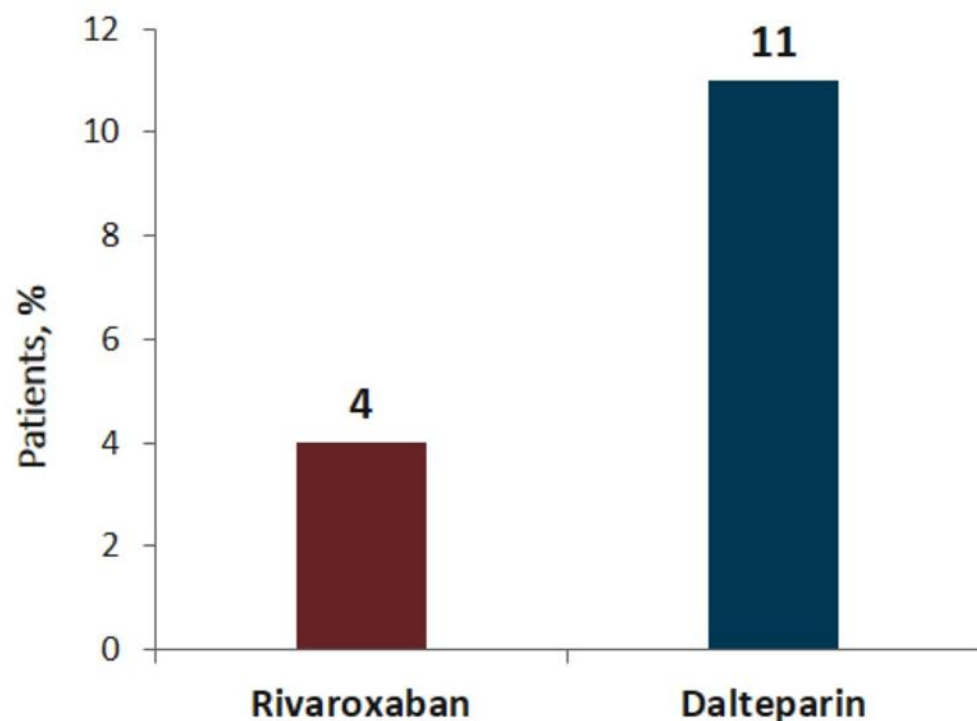
6 months vs 12 months
of treatment

Placebo

Primary efficacy: incidence of recurrent VTE

Secondary outcomes: safety, acceptability, biomarker identification, and health economics

SELECT-D Trial: Primary Endpoint



54% of patients completed 6 months of trial treatment

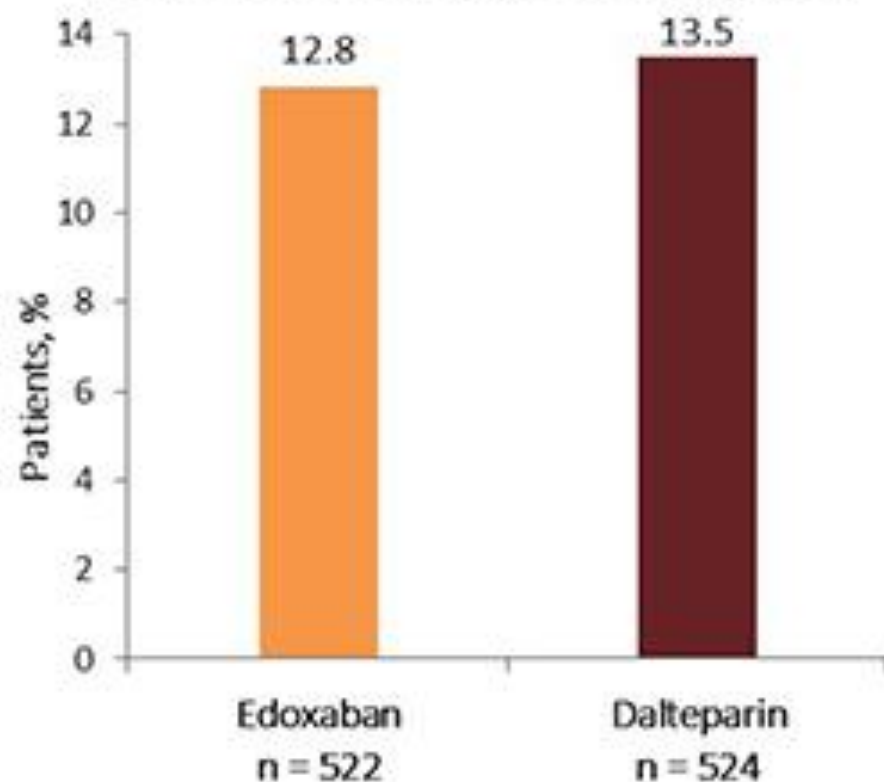
- 52% on dalteparin
- 55% on rivaroxaban

- N=406
- Major bleeds were similar: 3% with dalteparin, 4% with rivaroxaban

Hokusai VTE-Cancer, SELECT-D

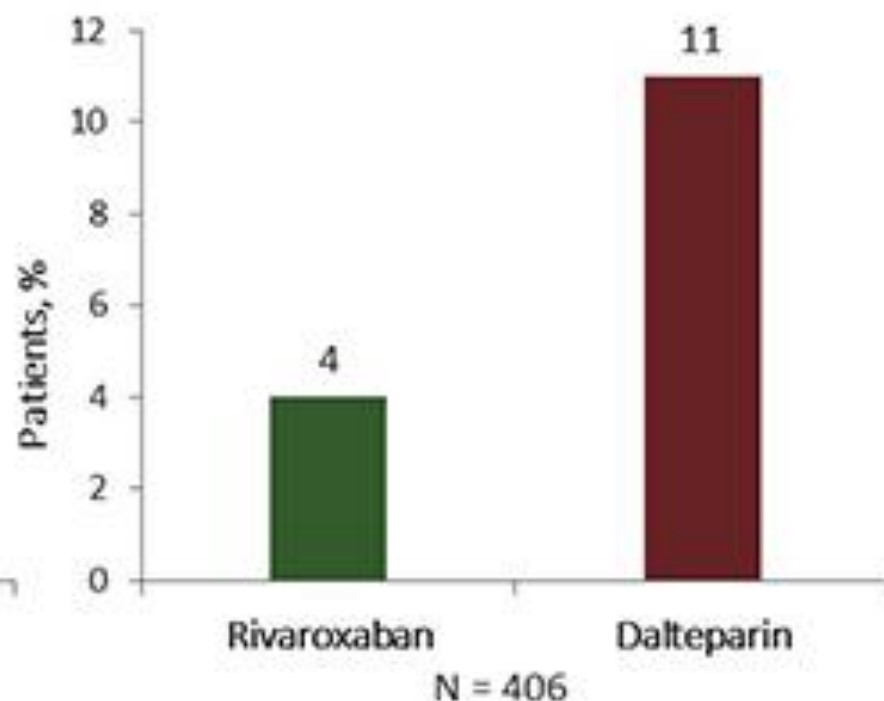
Hokusai VTE-Cancer^[a]

Primary outcome: Composite of the first recurrent VTE or major bleeding event



SELECT-D^[b]

Primary outcome: Recurrent VTE



a. Raskob GE, et al. ASH 2017. Abstract LBA-6.

b. Young A, et al. ASH 2017. Abstract 625.

Závěr.

- Edoxaban je alternativou v léčbě TEN u nemocných s nádorem
- Pacienti jsou ve vysokém riziku recidivy po 6 měsících standardní léčby
- Benefit pokračování léčby po 6 měsících převyšuje riziko krvácení
- Diskutovaná je otázka krvácení u nemocných s kolorektálním karcinomem

Děkuji za pozornost

