Anticoagulants oraux directs et thrombose associée au cancer

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Liens d'intérêt G Meyer

- Investigator: Bayer, Daichi-Sankyo, Sanofi Aventis, Leo Pharma
- Research Funding: Leo Pharma, Boehringer-Ingelheim, Bayer
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Recommandations

"For long-term anticoagulation, LMWH for at least 6 months is preferred because of improved efficacy over VKAs. VKAs are an acceptable alternative for long-term therapy if LMWH is not available. Evidence: strong"

Lyman G. *et al. J Clin Oncol* 2013; 31: 2189-204

"LMWHs are preferred over VKA for the early maintenance treatment (10 days to 3 months) and long-term treatment (beyond 3 months) of VTE in cancer patients [Grade 1A]."

Farge D. *et al. J Thromb Haemost* 2013; 11: 56–70.

"In patients with DVT of the leg and cancer, we suggest LMWH over VKA therapy (Grade 2B)."

Kearon C. et al. Chest 2012; 141 (supplement): e419-e494

The CLOT Study

Multicenter randomized open trial

672 patients with cancer and venous thromboembolism

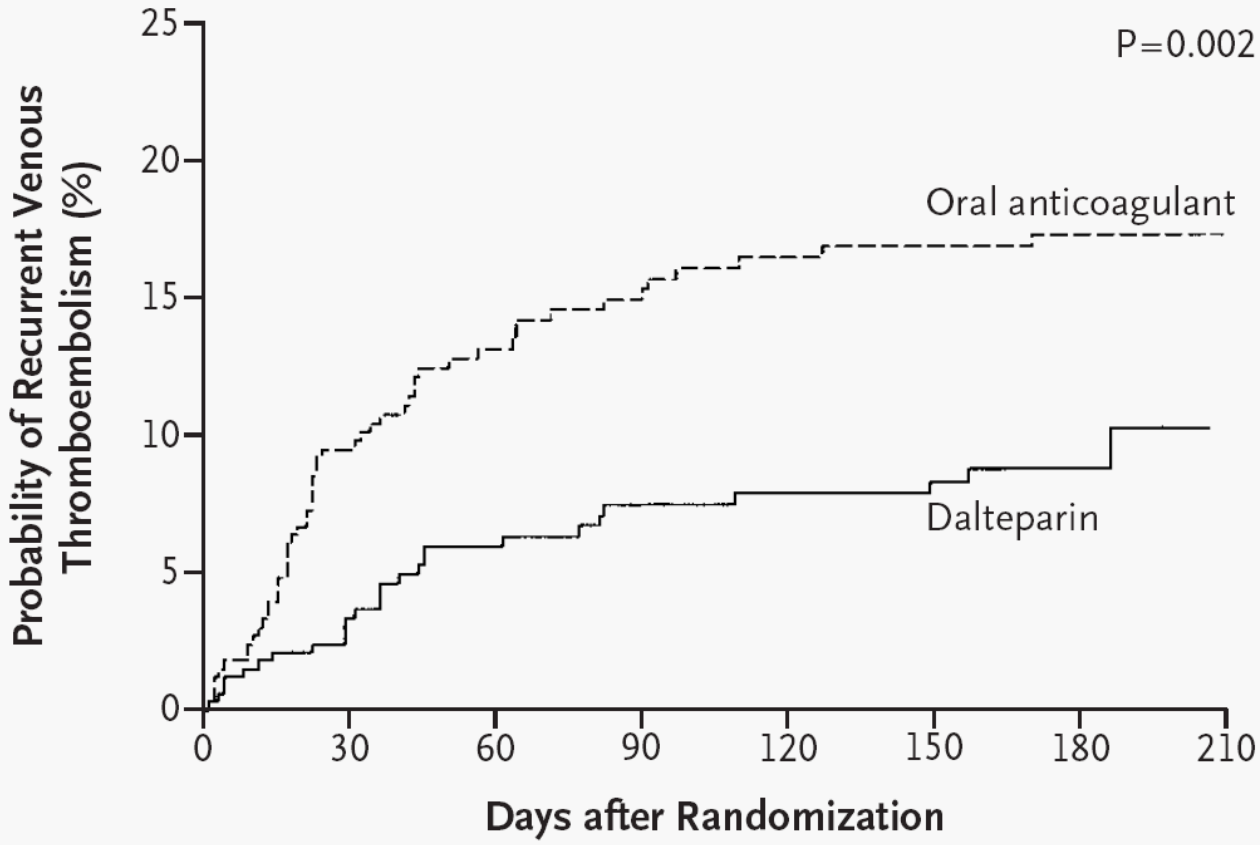
Dalteparin (n = 336): 200 IU/kg 1 month followed by 150 IU/kg 5 months

Warfarin (n = 336): INR 2.5 6 months

Major endpoint : objectively confirmed VTE recurrences.

Lee A. et al. *N Engl J Med* 2003; 349: 146-153

The CLOT Study

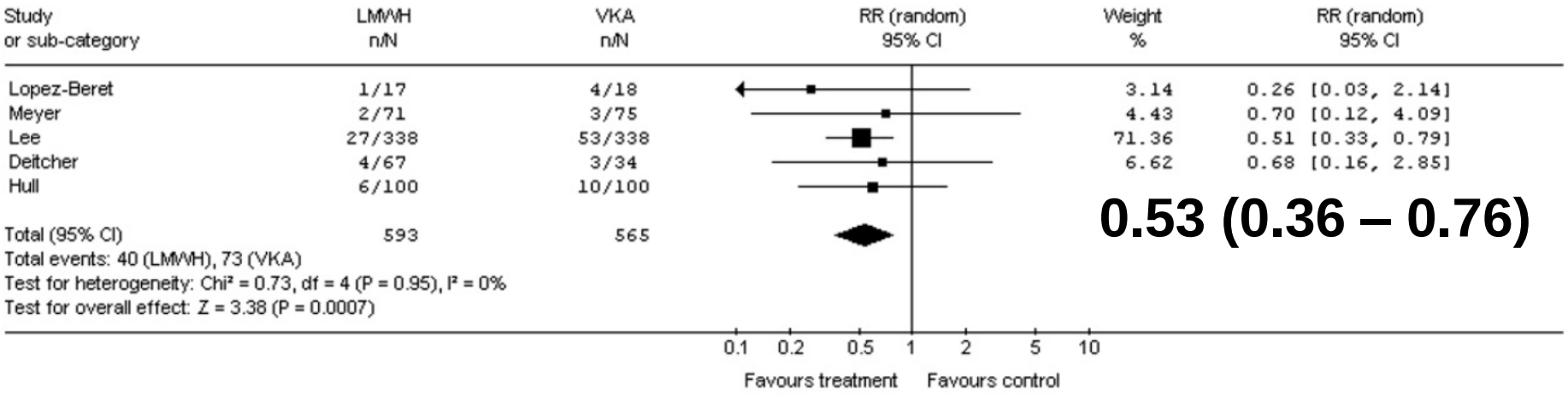


No. at Risk

Dalteparin	336	301	264	235	227	210	164
Oral anticoagulant	336	280	242	221	200	194	154

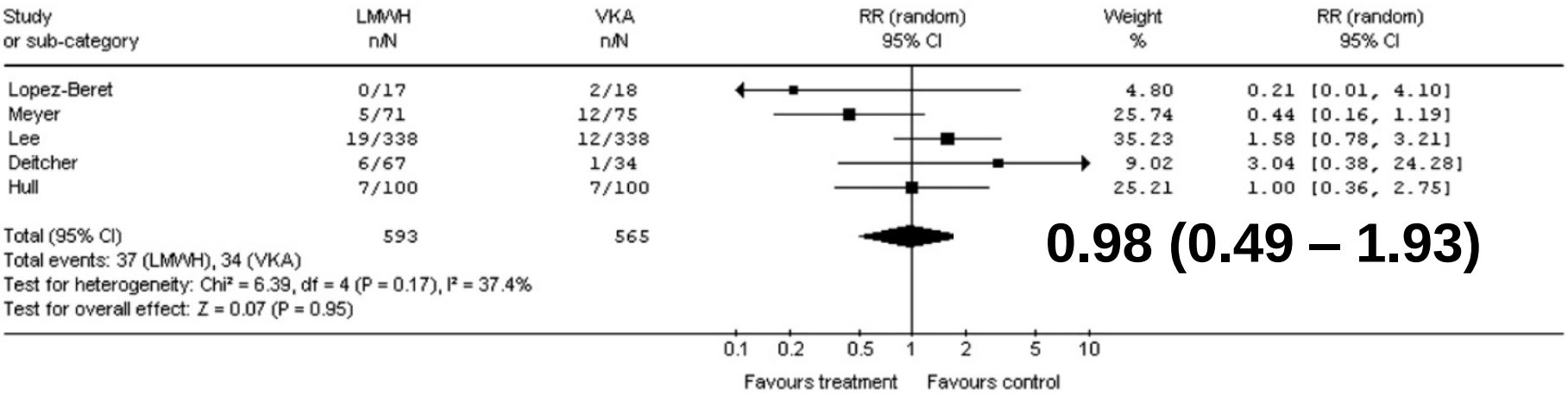
Lee A. et al. *N Engl J Med* 2003; 349: 146-153

La méta-analyse: efficacité



Louzada M. et al. *Thromb Res* 2009; 123: 837-844

La méta-analyse: sécurité



Louzada M. et al. *Thromb Res* 2009; 123: 837-844

Les médecins ne suivent pas les recommandations

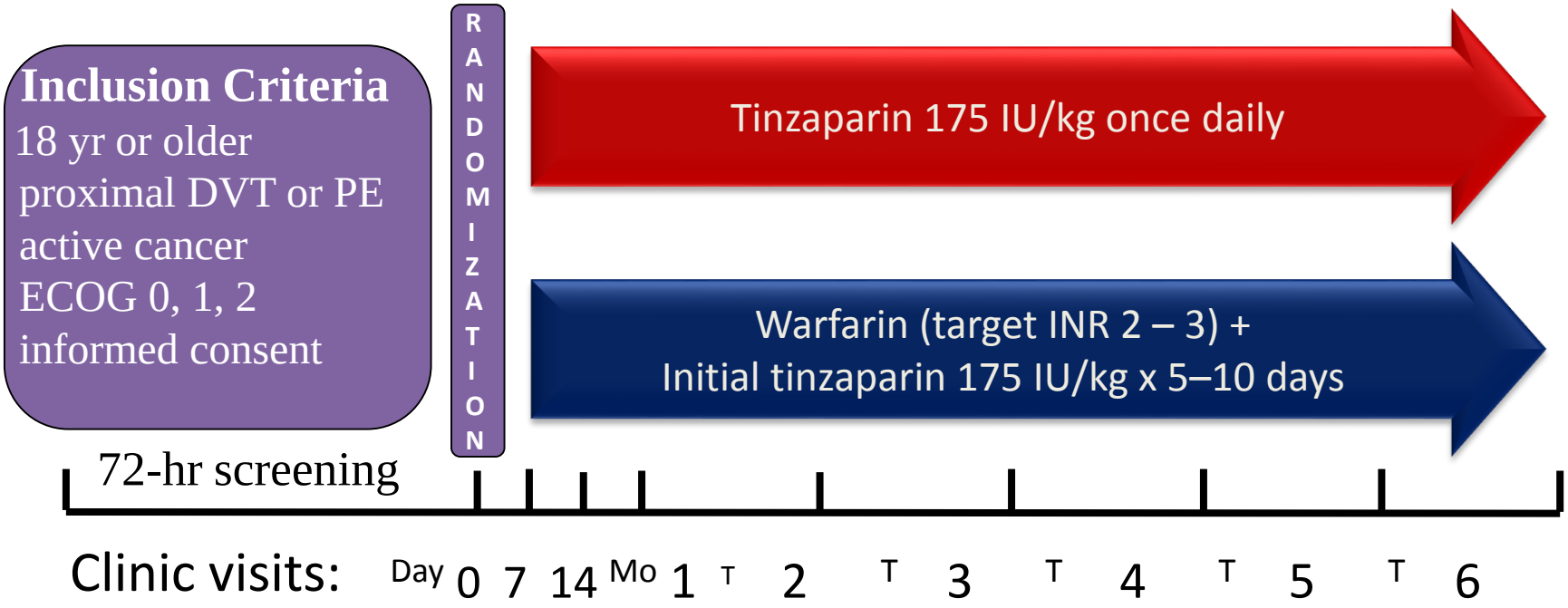
	VKA
Imberti (Italy); n = 424	64%
Gussoni (RIETE) n = 5483	32%
Spirk (Switzeland) n = 315	51%
Belhadj Chaidi (France) n = 145	23%
Kleinjan (International)* n = 141	18%

* Survey on 141 doctors

Imberti D. *et al. Haematologica* 2008 ; 93: 273-278.
Gussoni G. *et al. Thromb Res* 2013; 131: 24-30
Spirk D. et al. *Thromb Haemost* 2011; 105: 962–967
Belhadj Chaidi et al. *J Mal Vasc* 2013; 38: 185-92
Kleinjan A. et al. *Thromb Haemost* 2013 August 15

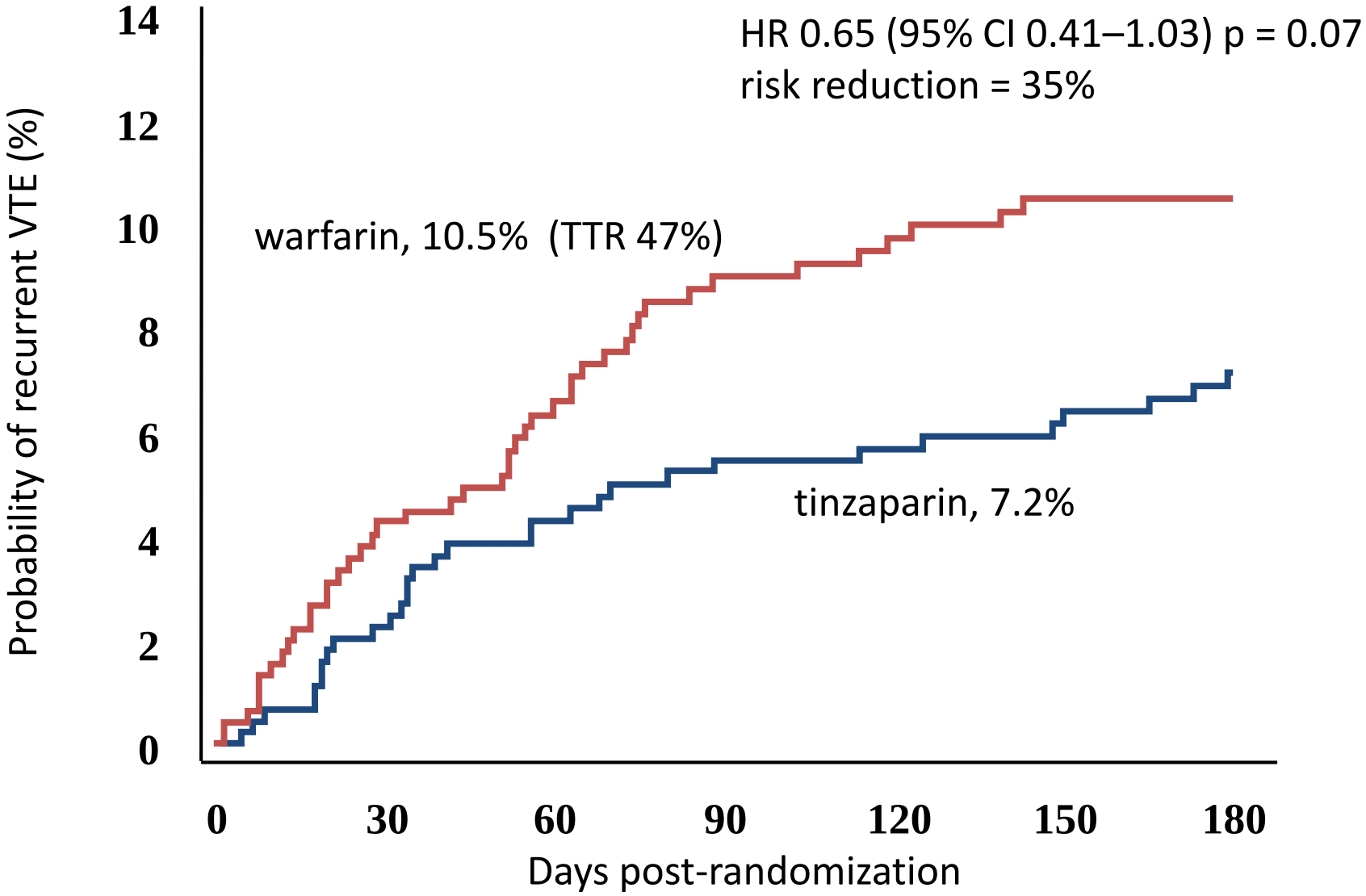
The CATCH study

Prospective, randomized open-label, with blinded central adjudication



Lee A. et al. *JAMA* 2015; 314: 677-86

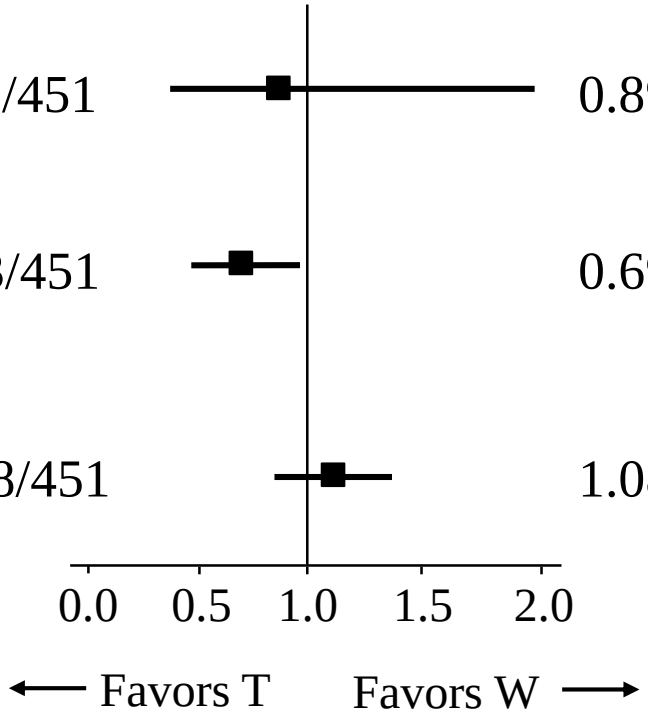
CATCH. Efficacité



Lee A. et al. *JAMA* 2015; 314: 677-86

CATCH. Sécurité

Event	Tinzaparin n/N	Warfarin n/N	HR	HR [95% CI]
Major bleeding	13/449	12/451		0.89 [0.40, 1.99]
Clinically relevant non-major bleeding	50/449	73/451		0.69 [0.49, 0.96]
Overall mortality	150/449	138/451		1.08 [0.85, 1.36]



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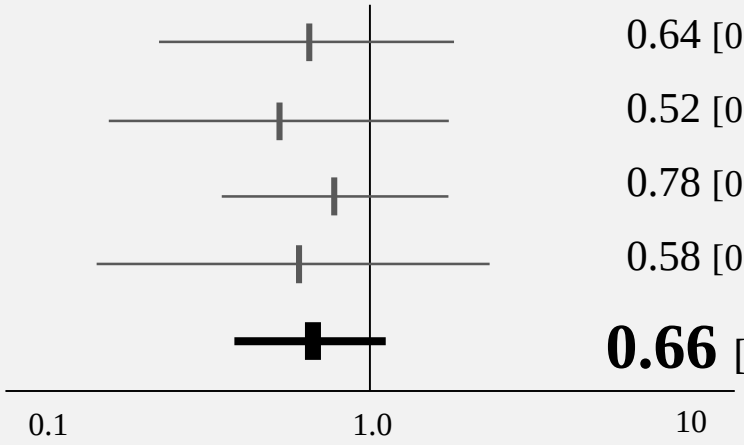
Problèmes liés au traitement prolongé par HBPM

- Injections
- Plaquettes
- Coût: 8.60 euros to 16.90 euros
- Infirmière
- Hématomes
- Récidives: 7%
- Hémorragies: 3-7%

AOD METV et cancer : méta-analyse

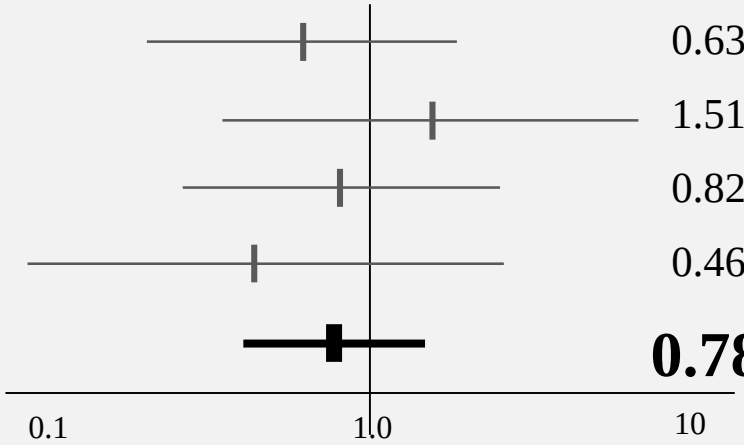
Rec ETE

	AOD	enox/AVK	RR [CI95%]
EINSTEIN	6/232	8/198	0.64 [0.23 ; 1.81]
HOKUSAI	4/109	7/99	0.52 [0.16 ; 1.72]
RECOVER	10/173	12/102	0.78 [0.35 ; 1.76]
AMPLIFY	3/81	5/78	0.58 [0.14 ; 2.34]
total	25/595	32/537	**0.66** [0.39 ; 1.11]



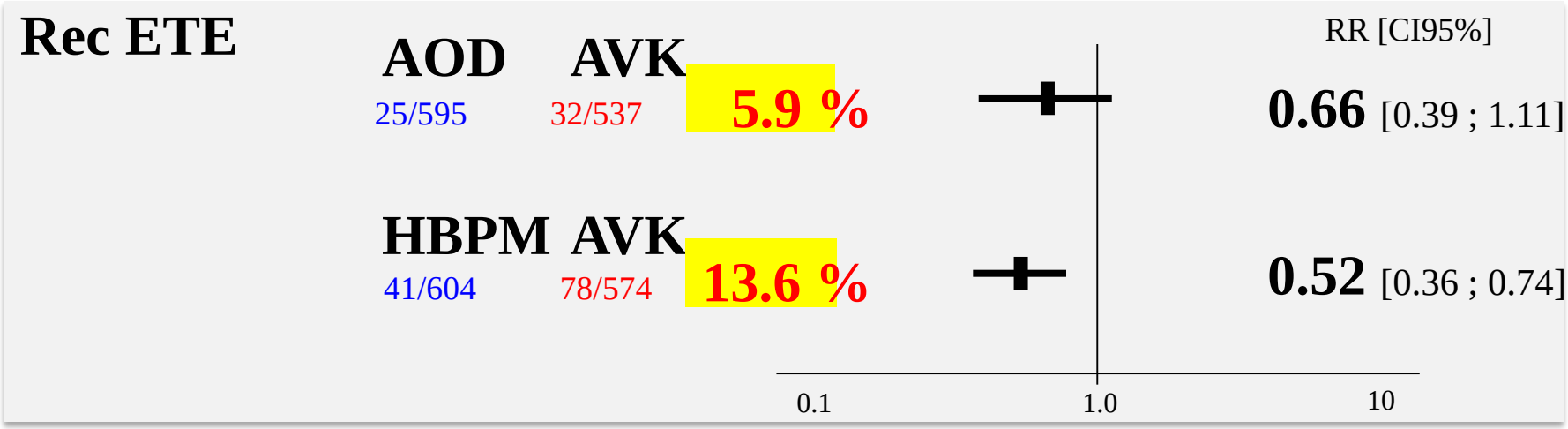
Hgie majeure

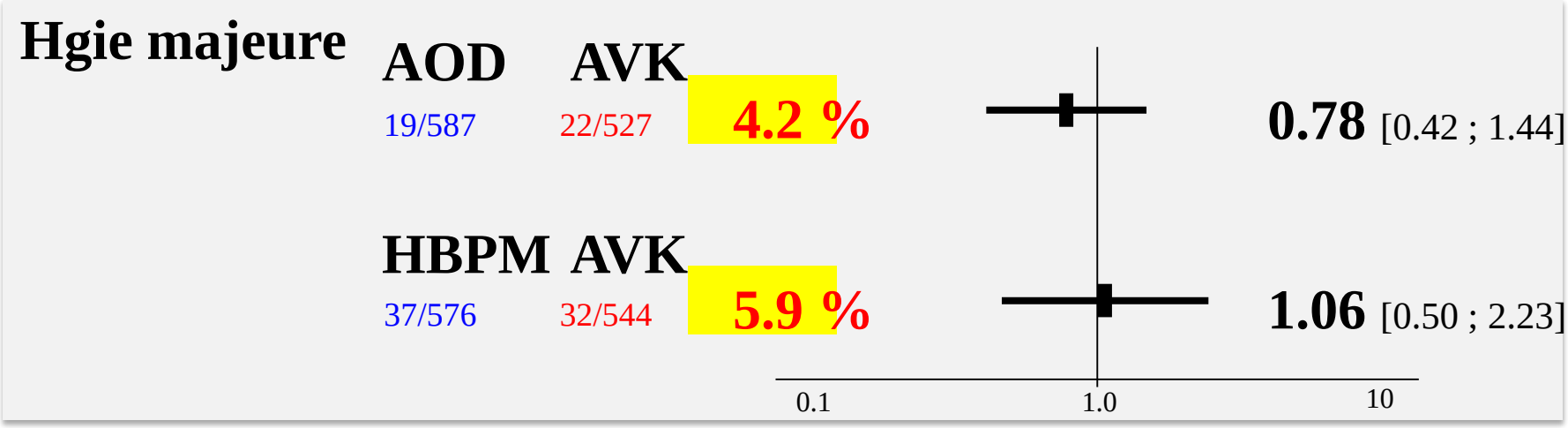
	AOD	enox/VKA	
EINSTEIN	6/232	8/196	0.63 [0.22 ; 1.79]
HOKUSAI	5/109	3/99	1.51 [0.37 ; 6.17]
RECOVER	6/159	7/152	0.82 [0.28 ; 2.36]
AMPLIFY	2/87	4/80	0.46 [0.09 ; 2.44]
total	19/587	22/527	**0.78** [0.42 ; 1.44]



Carrier M. et al. *Thromb Res* 2014;134:1214-9.

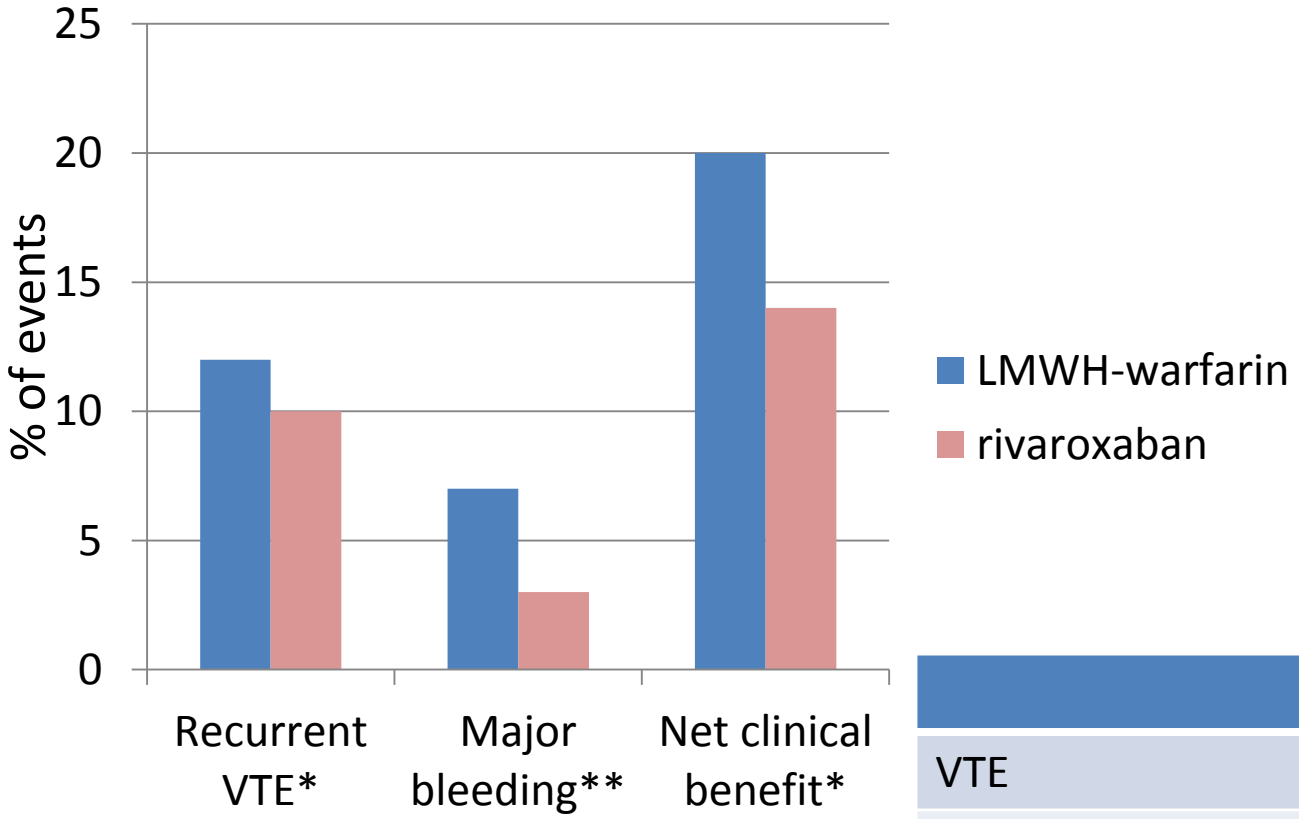
AOD METV et cancer : méta-analyse





Carrier M. et al. *Thromb Res* 2014;134:1214-9.

EINSTEIN : cancer actif à l'inclusion



*: ITT population, n = 462
**: safety population, n = 459

	Hazard Ratio (95% CI)
VTE	0.62 (0·21–1·79)
Major bleeding	0.47 (0·15–1·45)
Net clinical benefit	0.50 (0·24–1·03)

Prins M H. et al. *Lancet Haematol*. 2014; 1: e37–46

EINSTEIN, CLOT et CATCH: patients

	Einstein (n = 655)	CLOT (n = 672)	CATCH (n = 900)
Recurrent or metastatic cancer	22%	67.3%	54.7%
Anticancer treatment	13%*	77.7%**	42.4%***
% INR 2-3	57%-59%	46%	47%

*: chemotherapy,
**: all anticancer treatments,
***: systemic treatment (chemo or targeted therapy or hormonal treatment)

Lee A. et al. *N Engl J Med* 2003; 349: 146-153
Prins M H. et al. *Lancet Haematol*. 2014; 1: e37–46
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Conclusion

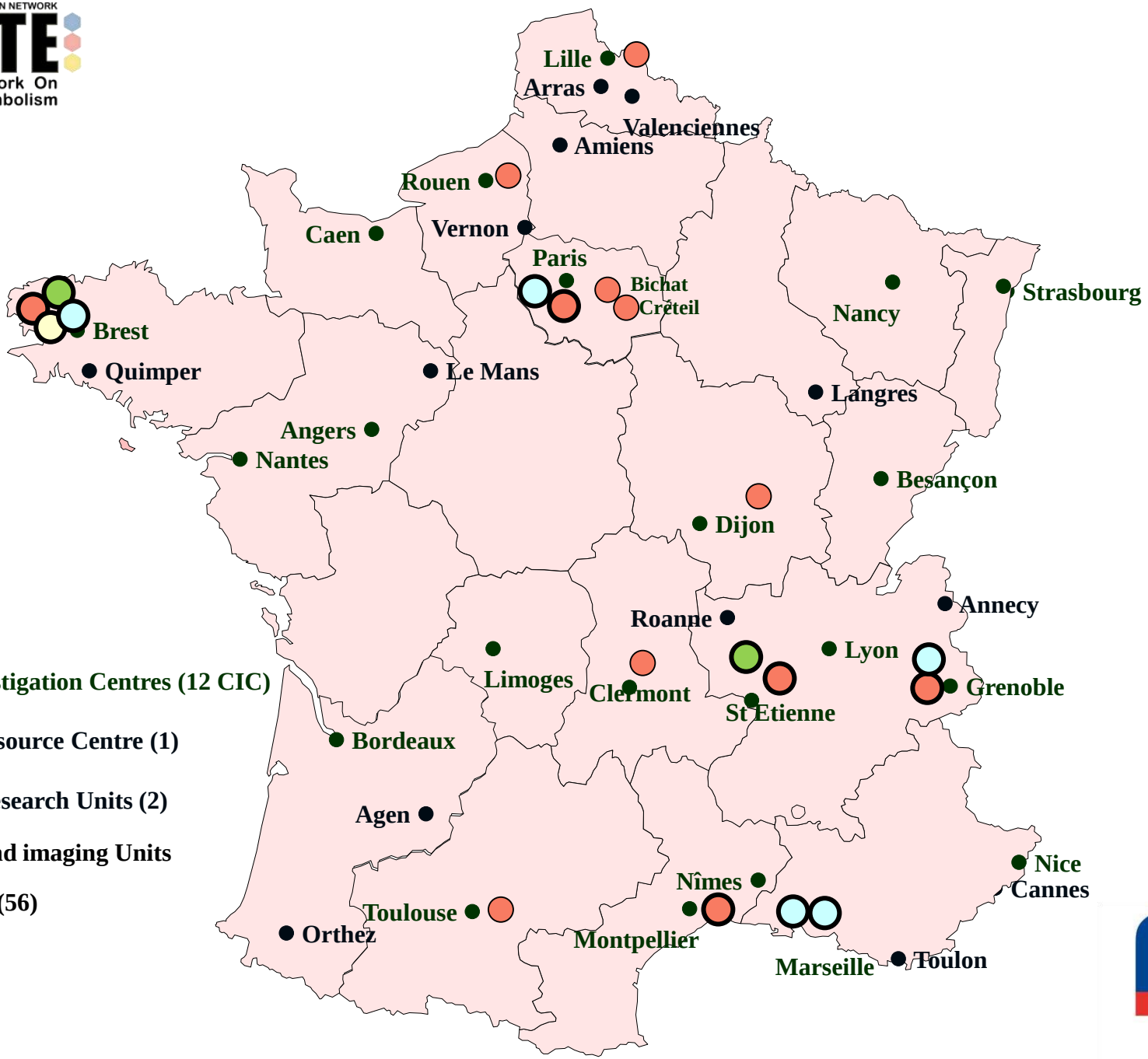
Des données encourageantes mais encore fragiles sur des patients sélectionnés et des cancers peu actifs

Pas de comparaison directe avec les HBPM

Interactions avec les drogues anti-tumorales?

Des études sont en cours

INNOVTE
F-CRIN NETWORK
INvestigation Network On Venous Thrombo-Embolism



- Clinical Investigation Centres (12 CIC)
- Biological Resource Centre (1)
- University Research Units (2)
- Biological and imaging Units
- Clinical sites (56)

fcrin