PARCOURS DU PATIENT AVEC THROMBOSE ASSOCIEE AU CANCER

- **Docteur Antoine ACHKAR**
- **Service de Pneumologie et Oncologie Thoracique**
- **Centre Hospitalier Intercommunal Poissy Saint Germain (CHIPS)**

BOLOGNE 24 Avril 2025

Cancer and VTE

Consensus ➔ Propositions

F-CRIN NETWORK

INNOVTE

INvestigation Network On Venous Thrombo-Embolism

F.CRIN

FRENCH CLINICAL RESEARCH INFRASTRUCTURE NETWORK

French Multidiciplinar Societies

Guidelines 2023

Respir. Med and Res 84 (2023) 101056

Original article

French guidelines for the treatment of cancer-associated venous thromboembolism - 2023 update

Endorsed by the Investigation Network On Venous Thrombo-Embolism (INNOVTE) and the French Speaking Society of Respiratory Diseases (SPLF)

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Propositions 2024

Archives of Cardiovascular Disease 117 (2024) 3–5

Scientific editorial

Management of cancer-associated thromboembolism: Introduction

Isabelle Mahé[a,c,e], Olivier Sanchez[b,c,e,*], Patrick Mismetti[d,e]

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Originality – unique

Thrombose associée au cancer : quand, comment et pourquoi ?

Comment gérer l'absence de preuve et de recommandation ?

29 NOV 2024

Cancer & Thrombose

Parcours patient et anticoagulation

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

G.I.T.A

AFSOS
Association Francophone des Soins Oncologiques de Support

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Syndrome de Trousseau 1865 : thrombose associée au cancer
TAC ou CAT

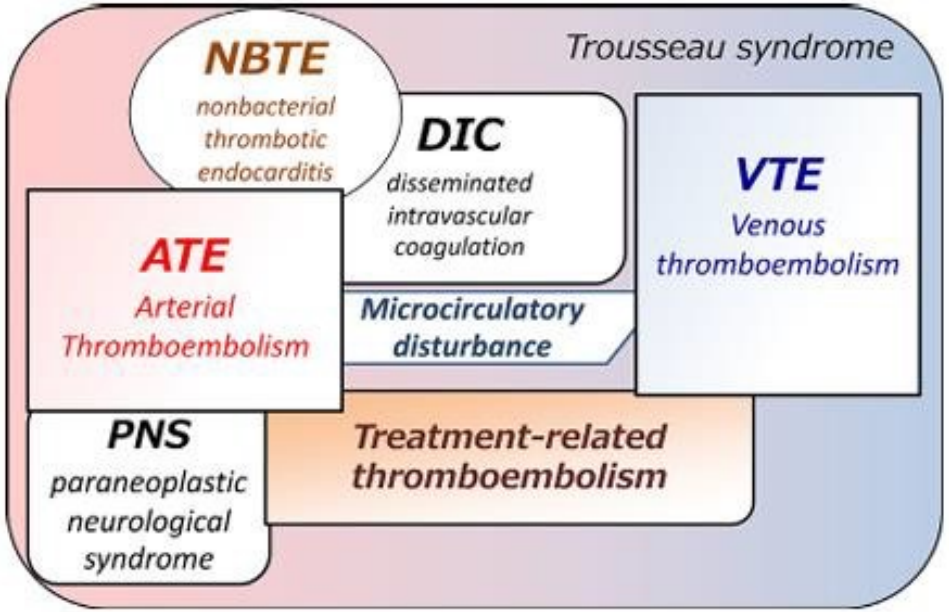


Fig. 1. Cancer-associated thrombosis. Thromboembolism that develops during cancer treatment is classified as arterial thromboembolism and venous thromboembolism, but multiple pathologies are considered depending on the onset mechanism. These thromboses are collectively referred to as cancer-associated thrombosis.

M. Mukai, T. Oka / Journal of Cardiology 72 (2018) 89–93

Diagnostic de CAT :

what next for practice?

- ***Où, Qui, quand, quoi comment?***
- ***Où ? Ville ou Hôpital?***

  Patients éligibles à une prise en charge ambulatoire
- ***Qui ? Quel spécialiste? Quelle organisation?***
- ***Quoi ? Situations auxquelles le patient/médecin doivent faire face?***
- ***Comment ? Quelle prise en charge, quelle stratégie thérapeutique?***

Quelle prise en charge thérapeutique ?

CAT : treatment decision

Archives of Cardiovascular Disease 117 (2024) 29–44

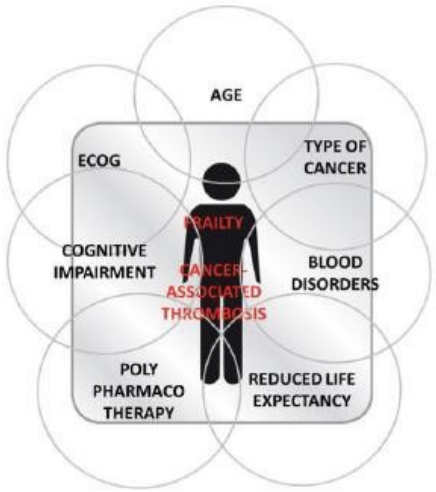
Disponible en ligne sur ScienceDirect www.sciencedirect.com

Elsevier Masson France EM|consulte www.em-consulte.com

Review

Anticoagulant treatment of cancer-associated thromboembolism

Isabelle Mahé[a,b,m,*,1], Didier Mayeur[c,1], Francis Couturaud[d,m], Florian Scotté[e], Ygal Benhamou[f,m], Asmahane Benmaziane[g], Laurent Bertoletti[h,m], Silvy Laporte[i,m], Philippe Girard[j,m], Patrick Mismetti[k,m,2], Olivier Sanchez[b,l,m,2], for the INNOVTE CAT Working Group[3]



PATIENT-RELATED

- Age
- Performance status
- Body weight
- Feasibility of oral route
- Renal function
- Platelet count

CANCER-RELATED

- Site
- Stage
- Progression
- Unresected tumour

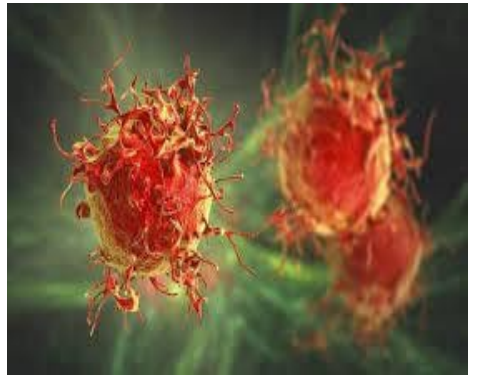
PATIENT PREFERENCE

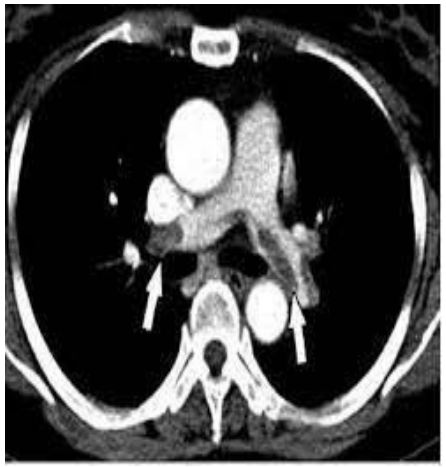
- Type (DVT or PE)
- Location
- Size
- Recurrence
- Incidental diagnosis
- Severity

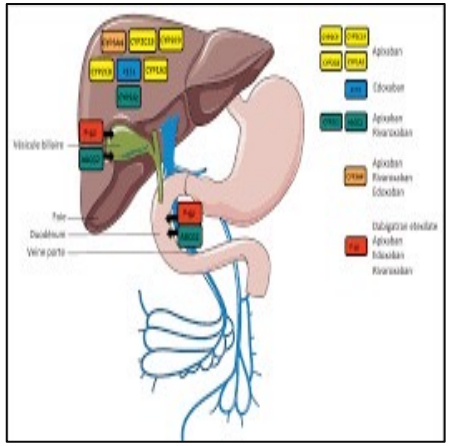
VTE-RELATED

- Drug-drug interactions

TREATMENT-RELATED





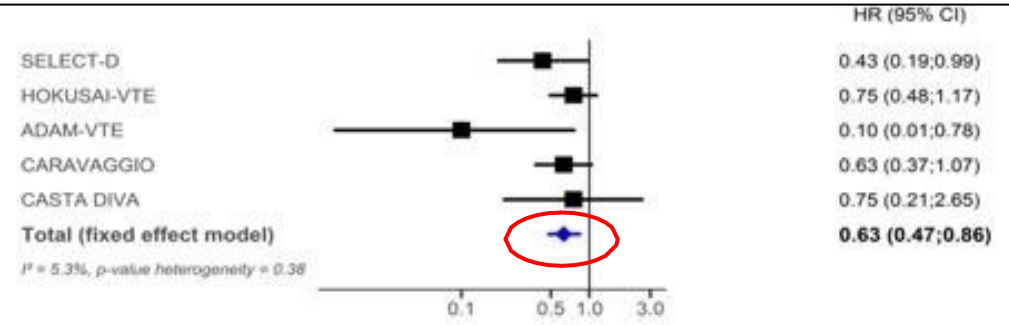


Mahé I et al. Arch Cardiovasc Dis 2024 ; 117 : 29-44

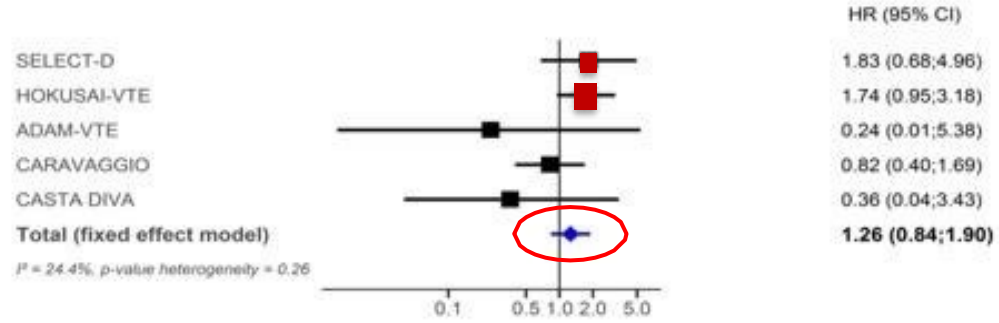
DOACs vs LMWHs : meta-analysis

Edoxaban, rivaroxaban and apixaban

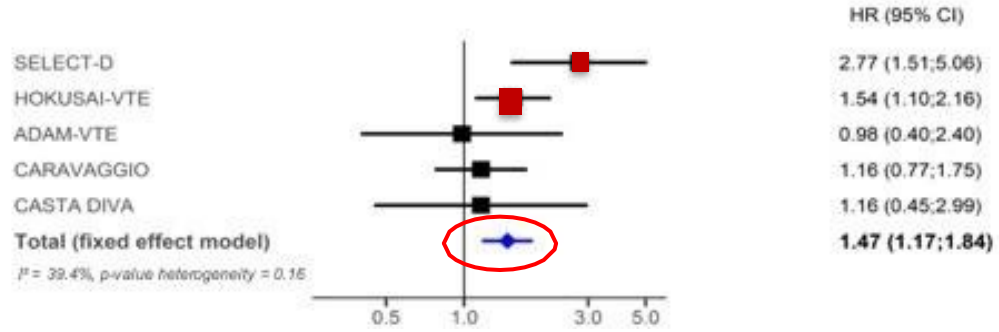
VTE Recurrence by 6 months

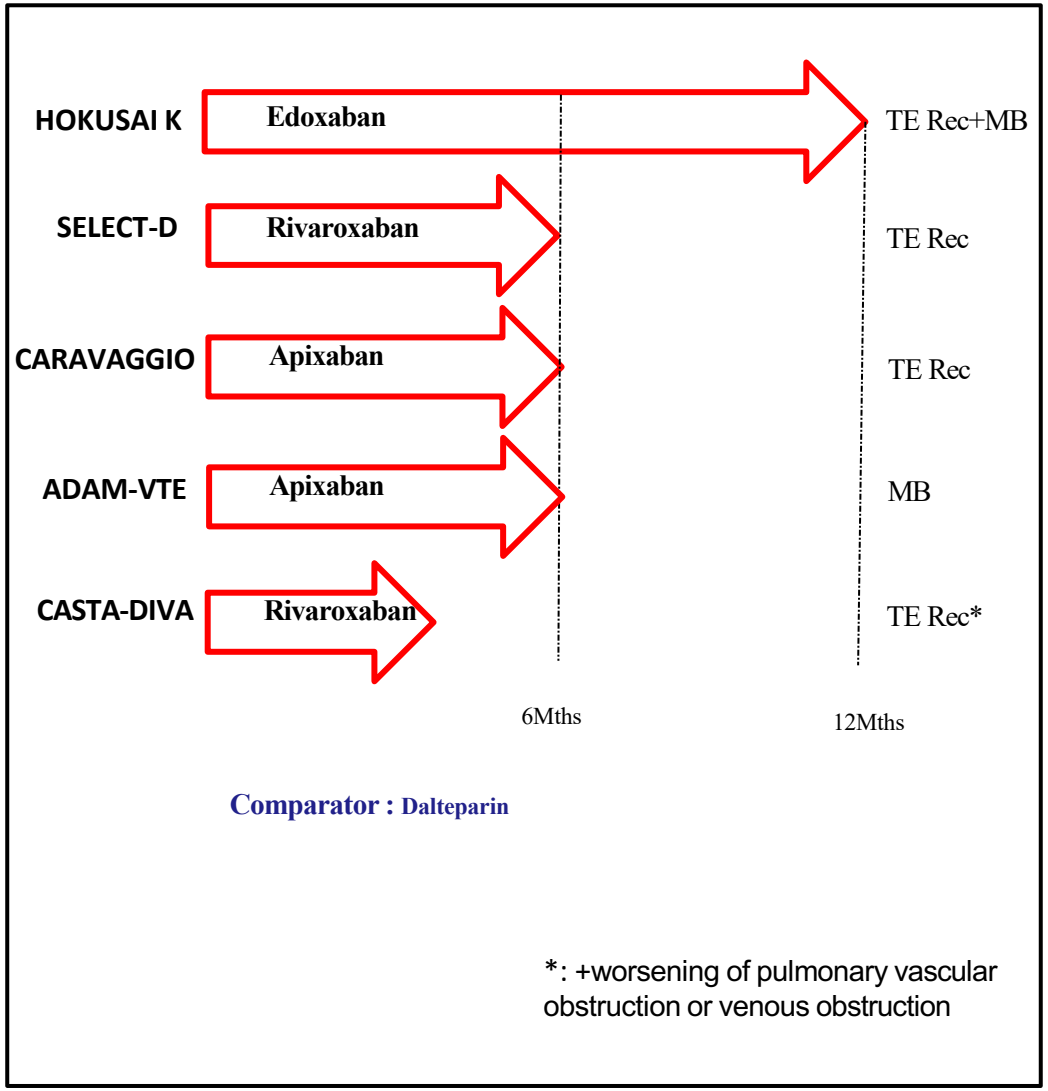


Major Bleedings by 6 months



CRB by 6 months





*: +worsening of pulmonary vascular obstruction or venous obstruction

Planquette B, et al. Chest 2021 :S0012-3692(21)04079-4

Proposals of the Expert Group for initial treatment

- **We recommend treating patients with active cancer diagnosed with proximal DVT or PE for at least six months.**
  - *Expert panel ranking: 3.77 out of 4.00*

- **When choosing the appropriate initial anticoagulant (LMWH or DXIs), we suggest considering the following, in collaboration with oncologists**
  - Type and severity of index VTE event
  - Perceived risk of bleeding (prefer drugs with shorter half-life if high-risk)
  - Ongoing anticancer treatment
    - Check for drug-drug interactions
    - Take into account planned surgery or invasive procedure.
  - Patient profile (age, platelet count, body weight, renal function, performance status)
  - Patient preference
  - *Expert panel ranking: 3.89 out of 4.00*

In patients with active cancer diagnosed with proximal DVT or PE

- **We recommend either apixaban or LMWH (without bridging with a VKA)**
- As an alternative, except for luminal GI tract cancer or urothelial cancer or renal cell carcinoma, we suggest edoxaban or rivaroxaban
- *Expert panel ranking: 3.33 out of 4.00*

Situations where an LMWH may be preferred over a DXI as initial CAT treatment

Settings where it may be more difficult to stop or control a MB or a CRB

Tumour site	Clinical setting
• **Oesogastric tumour or non-resected colorectal tumour**	With anaemia identified by iron deficiency or history of recent bleeding
• **Non-resected urothelial or gynaecological (especially cervical) cancer**	With anaemia identified by iron deficiency or history of recent bleeding
• **Metastasis of renal carcinoma or melanoma**	**If appearance on imaging is indicative of a risk of bleeding (hypervascularisation+++)**
• **Primary or secondary location close to large pulmonary vessels**	All clinical settings
• **Inoperable locally advanced breast cancer with skin involvement.**	With anaemia identified by iron deficiency or history of recent bleeding
• **Primary or secondary location of cutaneous tumours or sarcoma**	With anaemia identified by iron deficiency or history of recent bleeding

- **In all patients with CAT, during cancer treatment, we suggest to re-consider the type of anticoagulant treatment (LMWH vs DXI) periodically**
- *Expert panel ranking: 3.82 out of 4.00*

Mahé I et al. Arch Cardiovasc Dis 2024 ; 117 : 29-44

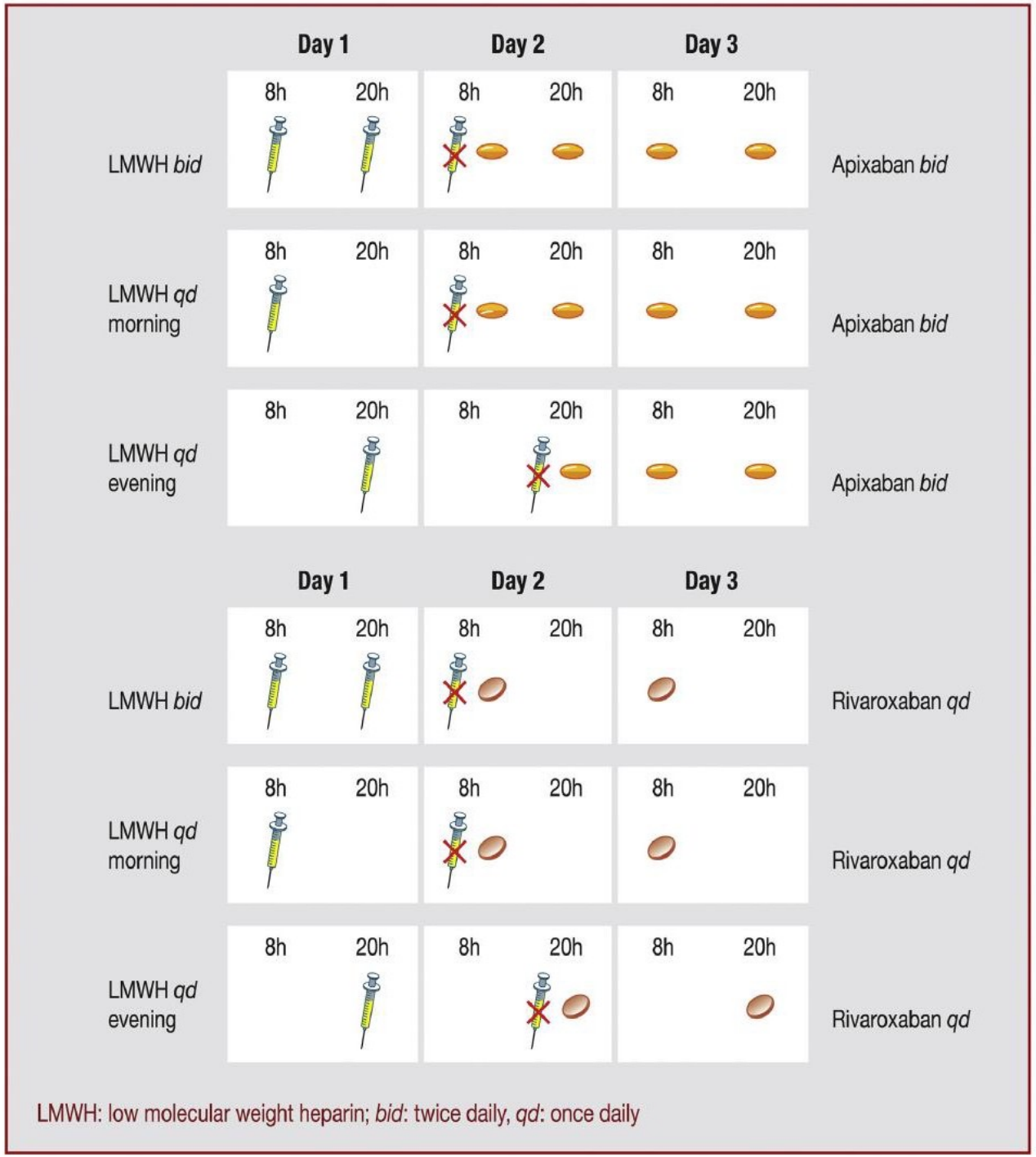
Anticoagulant switch

Proposals of the expert group

Anticoagulant switch

Reasons for switching anticoagulant therapy

- Initial decision by the clinician making the VTE diagnosis after discussion with the patient
- Acceptability, adherence and persistence issues and patient preference (whatever the reason)
- Intercurrent events during follow-up requiring specific management, such as surgery and other invasive procedures
- Initiation of an anticancer treatment with a potential for DDI
- VTE recurrence or bleeding
- Changes in the patient risk profile
- In case of regular nausea or vomiting



Mahé I et al. Arch Cardiovasc Dis 2024 ;17: 29-44

The balance risk of recurrence/risk of bleeding

Can we identify Ca-VTE patients at high risk of VTE recurrence?

Trials	Hokusai VTE cancer[20]	Select-D[21]	ADAM VTE[22]	Caravaggio[23]	CASTA DIVA[24]
DOACs	Edoxaban	Rivaroxaban	Apixaban	Apixaban	Rivaroxaban
LMWH	Dalteparin	Dalteparin	Dalteparin	Dalteparin	Dalteparin
N	1046	406	287	1155	158
Follow-up	12 months	6 months	6 months	6 months	3 months
VTE (%)*	6.5 vs. 8.8	3.9 vs. 8.8	0.7 vs. 6.3	5.6 vs. 7.9	6.4 vs. 10.1
	HR 0.75 (0.48-1.17)	HR 0.43 (0.19-0.99)	HR 0.099 (0.01-0.78)	HR 0.63 (0.37-1.07)	SHR 0.75 (0.21-2.66)
MB (%)*	5.6 vs. 3.2	5.4 vs. 3.0	0 vs. 1.4	3.8 vs. 4.0	1.4 vs. 3.7
	HR 1.74 (0.95-3.18)	HR 1.83 (0.68-4.96)	HR not estimable	HR 0.82 (0.40-1.69)	SHR 0.36 (0.04-3.43)
CRNMB (%)*	12.3 vs. 8.2	12.3 vs. 3.5	6.2 vs. 4.9	9.0 vs. 6.0	10.8 vs. 6.1
	HR 1.55 (1.05-2.28)	HR 3.76 (1.63-8.69)	NR	HR 1.42 (0.88-2.30)	NR
Mortality (%)*	26.8 vs. 24.2	23.6 vs. 27.6	16 vs. 11	23.4 vs. 26.4	25.7 vs. 23.8
	HR 1.14 (0.90-1.45)	NR	HR 1.40 (0.82-2.43)	HR 0.82 (0.62-1.09)	HR 1.05 (0.56-1.97)

*Rates are DOAC versus LMWH, at 6 months except for CASTA DIVA where follow-up was 3 months; HR is followed by 95% confidence interval in the parenthesis.
Abbreviations: CRNMB, clinically relevant non-major bleeding; DOAC, direct oral anticoagulant; HR, hazard ratio; LMWH, low-molecular weight heparin; MB, major bleeding; NR, not reported; SHR, subdistribution hazard ratio; VTE, venous thromboembolism.

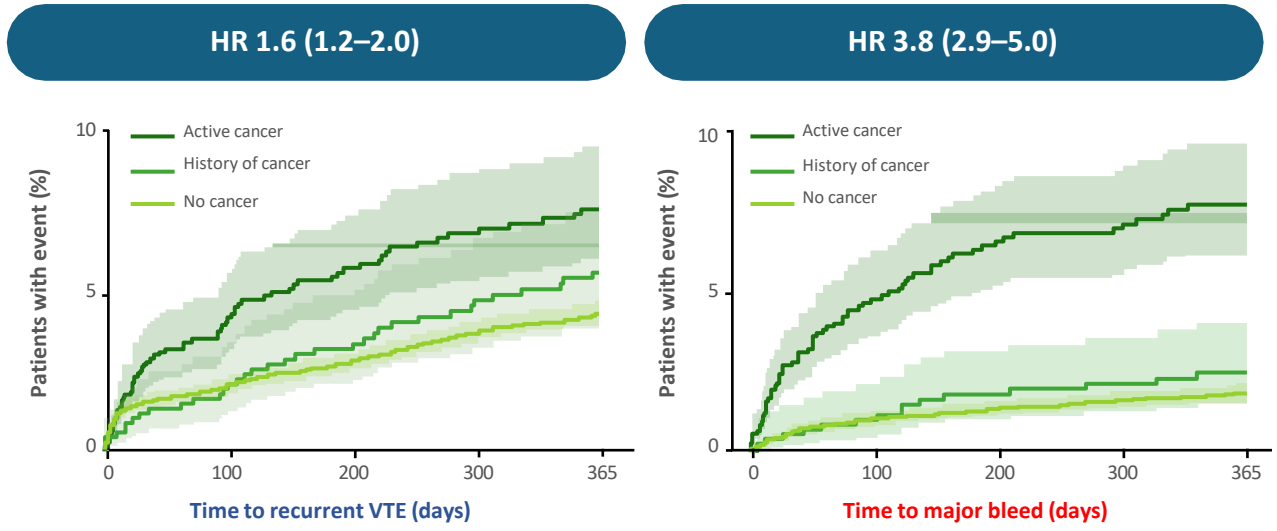
Randomized controlled trials of DOACs versus LMWH

N Engl J Med 2013;369:1406-15; J Clin Oncol 2018 Jul 10;36(20):2017-2023; J Thromb Haemost 2020 Feb;18(2):411-421; N Engl J Med 2020;382:1599-607; CHEST 2020 Feb;18(2):411-421

Risk of VTE recurrence in patients with active cancer, cancer history, and no cancer history

GARFIELD-VTE

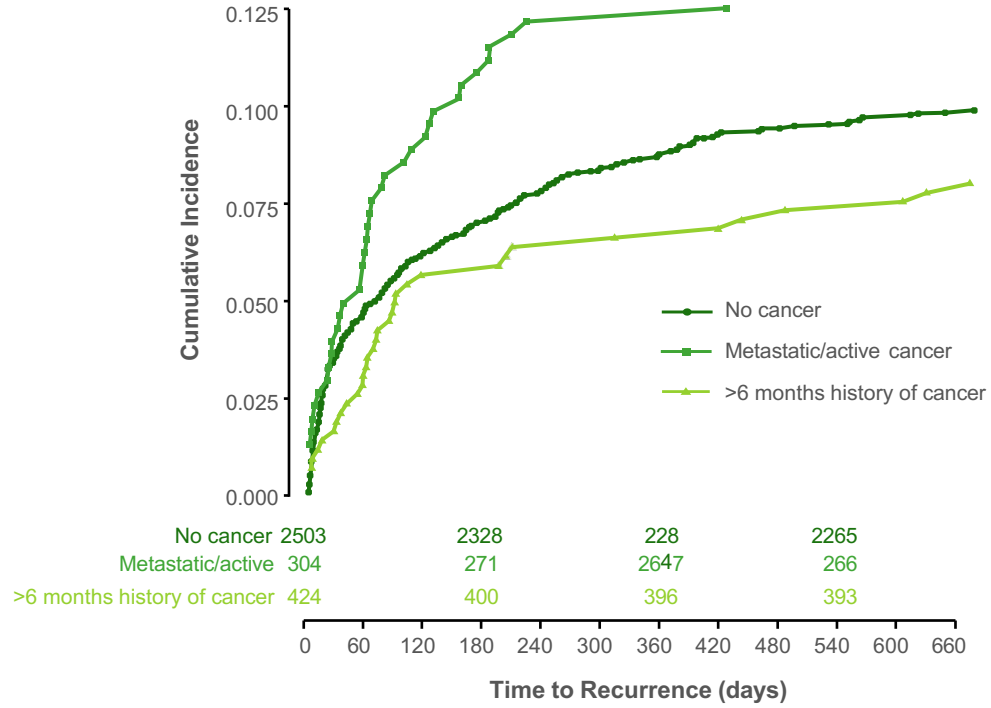
- Prospective, observational study of 10,684 patients with objectively diagnosed VTE from 415 sites in 28 countries
- 1075 patients with active cancer (lung (14.5%), colorectal (11%), breast (10.6%), gynaecological (10.3%)
- 674 patients with a history of cancer, and 8935 patients without cancer



Weitz J et al, J Thromb Thrombolysis 2020; 50; 267-277

General population of Oklahoma County

- Population-based prospective study
- Cumulative incidence of the first recurrent venous thromboembolic event amon adults age ≥ 18 years detected during the surveillance period among all incident events (n = 3231)
- Stratified by cancer history : active cancer, history of cancer >6 months prior to diagnosis of VTE



Raskob G, Wendelboe A, Campbell J, et al. J Thromb Haemost 2022;20:2366-78.

Risk of VTE recurrence in patients with active cancer, cancer history, and no cancer history

CAT and risk of VTE recurrence

➢ Situations associated with a low risk of VTE recurrence

- Patients with cancer who had undergone successful cancer surgery within the three months prior to the VTE index event and not requiring adjuvant therapy (ie, the main risk factor for VTE could be surgery rather than cancer)

➢ Situations associated with an intermediate risk of VTE recurrence

- Patients with a history of cancer

➢ Situations associated with a high risk of VTE recurrence

- Patients with active cancer
  As the definition of "active cancer" varies across studies, the ISTH proposed a consensual definition:
  - No potentially curative treatment has been received
  - Evidence that curative treatment has not been effective (e.g. recurrent or progressive disease)
  - Ongoing treatment

Bleeding risk assessment according to guidelines

The patient's bleeding risk should be assessed

It should be reassessed periodically
Once a year in patients at low risk, and every 3 or 6 months in patients at a high risk for bleeding

Bleeding risk assessment should be used to identify and treat modifiable bleeding risk factors

Assessment may influence decision-making on the duration and regimen/dose of anticoagulant treatment

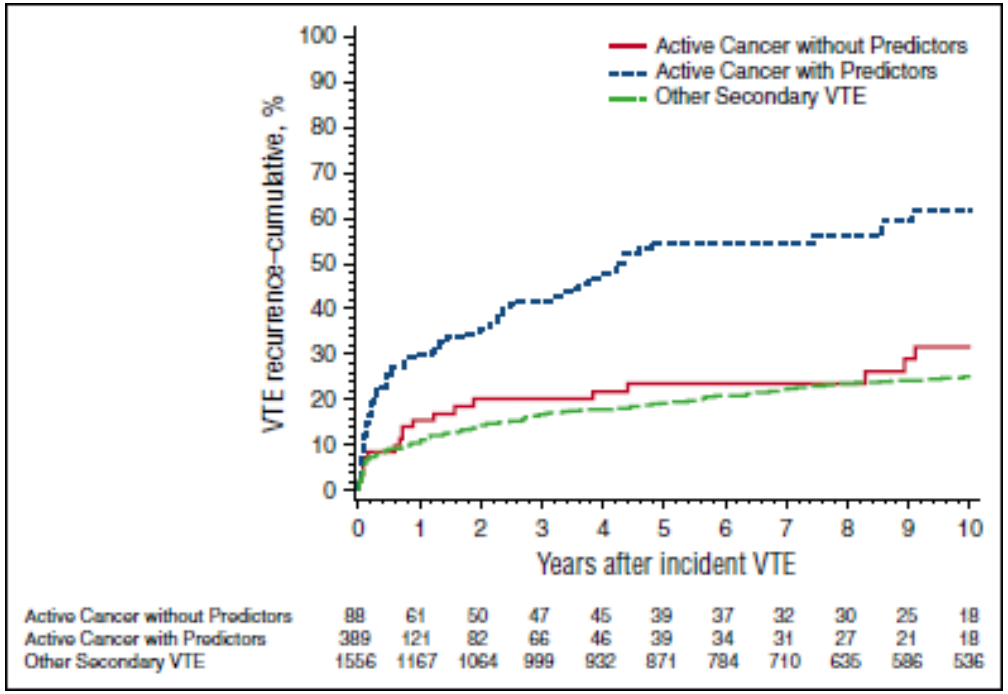
Mahé I et al. Arch Cardiovasc Dis 2024 ; 117:29-44.

Konstantinides SV, et al. Eur Heart J. 2020;41:543–603.

Kearon C, et al, J Thromb Haemost 2016;14:1480–3

CAT et traitement prolongé

Cumulative incidence of first VTE recurrence among Olmsted County, Minnesota, residents with incident DVT or PE, 1966-2000, associated with active cancer and one or more predictor of VTE recurrence, active cancer and no predictor, and noncancer secondary VTE.

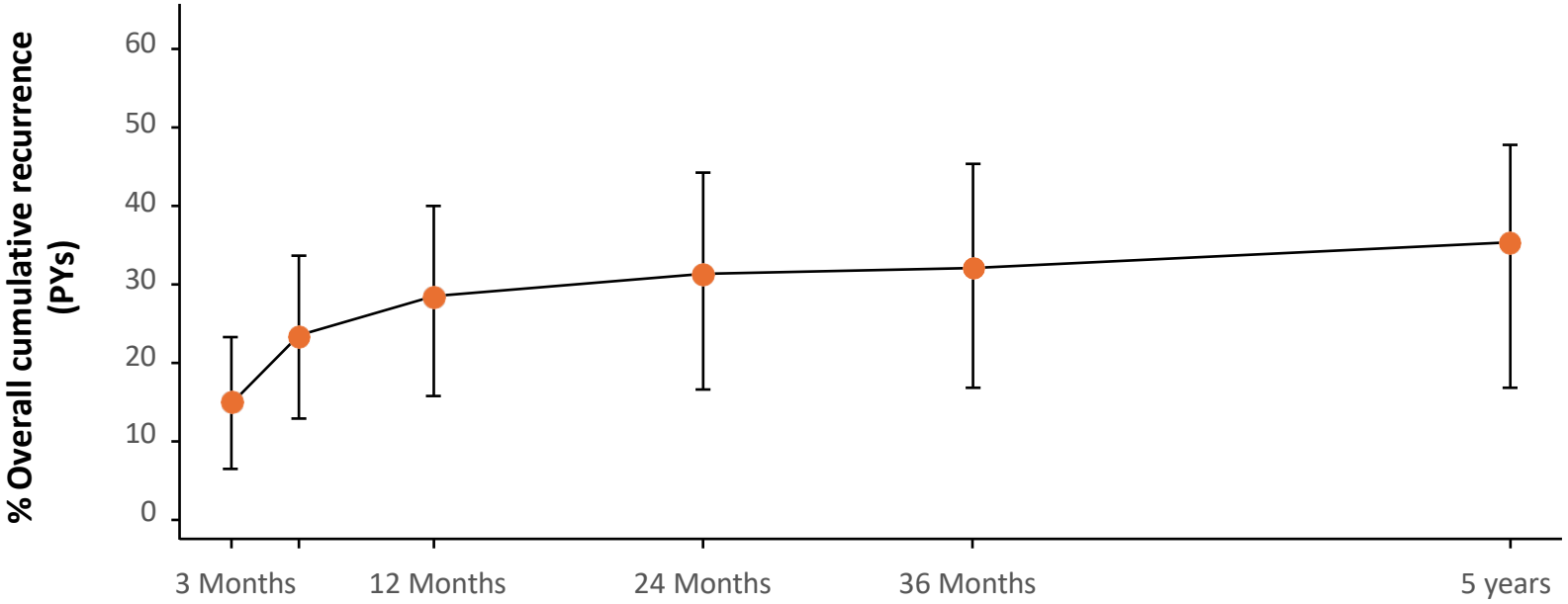


Chee, Blood 2014

The risk of VTE recurrence increases following anticoagulant discontinuation

- **Meta-analysis of 14 studies involving 1922 patients with cancer and a first VTE, who completed at least 3 months of anticoagulant therapy**, were followed after discontinuation of anticoagulant therapy, and with symptomatic recurrent VTE as an outcome during follow-up
- **Primary outcome : rate of recurrent VTE after discontinuation of anticoagulant therapy**

The cumulative VTE recurrence rate after discontinuation of anticoagulant therapy*



Recurrent VTE per 100 person-years after discontinuation of anticoagulant therapy: 14.6 events (95% CI: 6.5, 22.8) at 3 months

The cumulative VTE recurrence rate after discontinuation of anticoagulant therapy:

- 28.3% (95% CI 15.6, 39.6%) at 1 year
- 31.1% (95% CI 16.5, 43.8%) at 2 years
- 31.9% (95% CI 16.8, 45.0%) at 3 years
- 35.0% (95% CI 16.8, 47.4%) at 5 years

The sensitivity analysis based on studies in which the decision to stop anticoagulant therapy was not influenced by stratification of the risk of VTE recurrence
(i.e. absence of residual DVT on compression US) **showed similar results to the main analysis**

**Bars represent 95% credible intervals.

Marte A. M. van Hylckama Vlieg; ClinicalMedicine 2023;64: 102194

Perspective: improve the benefit-risk ratio

This raises the question of:
whether anti-coagulant treatment should be continued beyond the minimum recommended duration of six months

for ALL patients with CAT

Treatment beyond six months

- Discontinue anticoagulation?
- Continue anticoagulation at curative dose?
- Continue anticoagulation at a reduced dose?

Proposals of the Expert Group for extended treatment

- Beyond six months of CAT treatment, we recommend anticoagulant treatment continuation:
  - EITHER In case of active cancer including increased biomarkers, and planned continuation of anticancer treatment (including hormonotherapy) for the next six months
  - OR In case of VTE recurrence during the first six months of treatment.
  - *Expert panel ranking: 3.63 out of 4.00*

- When anticoagulant treatment is continued beyond six months, we recommend using a DXI, or LMWH if well tolerated, effective and accepted by the patient.
  - Pending results of ongoing research, we suggest not using reduced doses of DXIs.
  - *Expert panel ranking: 3.60 out of 4.00*

- In patients who no longer have an active cancer, we suggest considering the following when choosing the appropriate long-term anticoagulant strategy (stop, switch, reduced dose), in collaboration with oncologists
  - Risk of cancer recurrence, if in remission
  - Ongoing anticancer treatment, if any
  - Type, tolerability and acceptability of anticoagulant treatment during the first 6 months
  - Type and severity of index VTE event
  - Patient profile (age, platelet count, body weight, renal function)*
  - *Expert panel ranking: 3.70 out of 4.00*

Situations associated with a low risk of VTE recurrence
• Patients with cancer who had undergone successful cancer surgery within the three months prior to the VTE index event and not requiring adjuvant therapy (*ie*, the main risk factor for VTE could be surgery rather than cancer)
Situations associated with an intermediate risk of VTE recurrence
• Patients with a history of cancer
Situations associated with a high risk of VTE recurrence
• Patients with active cancer As the definition of "active cancer" varies across studies, the ISTH proposed a consensual definition[a]: ***Cancer is considered active if any of the following apply***: ○ No potentially curative treatment has been received ○ Evidence that curative treatment has not been effective (e.g. recurrent or progressive disease) ○ Ongoing treatment

Cancer activity and the risk of VTE recurrence

Mahé I et al. Arch Cardiovasc Dis 2024 ; 117 : 29-44

Trials	Einstein Choice	Amplify Ext	Renove	API-CAT
DOACs	Reduced dose rivaroxaban	Reduced dose apixaban	Reduced dose apixaban-rivaroxaban > 6 months	Reduced dose apixaban > 6 months
Comparator	Full dose rivaroxaban and Aspirin 100	Full dose apixaban and placebo	Full dose apixaban-rivaroxaban	Full dose apixaban
N	3396 (2,4 vs 2,3 vs 3,3) with cancer	2482 (1,8 vs 1,1 vs 2,2%) with cancer	2768 (10,1 vs 9,3%) with cancer	1766
Follow-up	18-24 M	18-24 M	37 M	11,8 M
VTE (%)	2,4 vs 3,2 vs 9,2 (U > P)	1,7 vs 1,7 vs 8,8	2,2 vs 1,8 p 0,23	2,1 vs 2,8 p 0,001
MB (%)	0,4 vs 0,5 vs 0,3	0,2 vs 0,1 vs 0,5	2,1 vs 4,0	2,9 vs 4,3
CRNMB (%)	2 vs 2,7 vs 1,8	3 vs 4,2 vs 2,7	8,6 vs 11,5	10 vs 12,3
Mortality (%)	0,2 vs 0,7 vs 0,6	2,4 vs 2,5 vs 10,4	4,3 vs 6,1	17,7 vs 19,6

Comparison of randomized controlled trials of DOACs in patient with or without active cancer

Einstein choice : patients with provoked and unprovoked index events; N Engl J Med 2017;376:1211-22
Amplify Ext : patients was participated in Amplify study with unprovoked index events; N Engl J Med 2013;368:699-708
Renove : patients with unprovoked, recurrent VTE, persistent risk factors or high risk of recurrence; *Lancet* 2025; 405: 725–35
API-CAT : patients with active cancer and proximal DVT or EP; N Engl J Med 2025;392:1363-73.

Un petit mot de contexte

- Vulnérable ≠ fragile : ?
  - La notion de patients fragiles dans les essais : Age > 75 ans – poids <60 kg et le rein
  - Que faire du patient thrombopénique, du patient obèse ?
  - Fragilité au sens gériatrique est différente de celle des essais
- Le problème est ailleurs :
  - clairance <30 ml/min voire moins
  - Age > 80 ans
  - poids <50 kg
- Un peu de données en MTEV hors cancer :
  - % de personnes agées, de petits poids, de rein, notion de patients vulnérables
- Très peu de données en MTEV ET CANCER

Essais cliniques randomisés des inhibiteurs du facteur Xa par voie orale et des héparines de bas poids moléculaire chez des patients atteints de cancer.

Étude[a]	*n*	Âge ≥ 75 ans	Clearance de la créatinine (Cockcroft-Gault) ≤ 50 mL/min	Poids ≤ 60 kg
SELECT-D (Young et al.) [7]	406	83 (20 %)	ND	62 (15 %)
CASTA DIVA (Planquette et al.) [8]	158	55 (35 %)	20 (13 %)	43 (27 %)
HOKUSAI CANCER (Raskob et al.) [9]	1050	176 (17 %)	72 (7 %)	159 (15 %)
CARAVAGGIO (Agnelli et al.) [10]	1155	348 (30 %)	314 (27 %)	112 (10 %)

Propositions

Patients âgés

Patients âgés

2.5.2. Recommandations de traitement

- Nous recommandons de traiter les patients âgés atteints de cancer qui présentent une CAT avec un **anticoagulant à la dose thérapeutique standard**.
- Nous recommandons de ne pas prendre en compte l'âge en tant que tel dans le choix du traitement anticoagulant entre les DXI et l'HBPM.
- Nous recommandons **d'évaluer et de prendre en compte les facteurs de fragilité** avec la règle des 6 C :
    - pour **choisir le traitement anticoagulant** (DXI ou HBPM),
    - éliminer les facteurs de risque de saignement, lorsque cela est possible,

Patients âgés

Règle des 6C

6 Cs checklist: features to be taken into account in older patients receiving therapeutic anticoagulant therapy.

Geriatric features	Evaluation	Management	Anticoagulant treatment	Treatment proposal[a]
Cachexia (malnutrition)	Weight loss > 5% in 1 month or > 10% en 6 months OR Albuminaemia < 35 g/L	Dietary advice Oral nutritional supplements (energy intake of 30 to 40 kcal/kg/d, protein intake: 1.2 to 1.5 g/kg/day)	If hypoalbuminaemia is present, bleeding risk may be increased during DXI treatment	Prefer LMWH throughout malnutrition period
Cognition (neuro-cognitive disorders)	MMSE < 24/30 Memory impairment screen (forgetting a word after 10 minutes in spite of prompting) [33,34]	Pill organiser Home nurse visits		If adherence is an issue, LMWH administered by a nurse at the patient's home may be of interest
Coming a cropper (falls)	Risk of falls in case of Standing on one foot < 10 sec Timed up and go test > 20 sec Five times sit to stand test > 15 sec	Physiotherapy Vitamin D Mobility aids Home improvement Remote assistance	Falls are not a contraindication to anticoagulants	No impact on medication choice
Comedication	Check for drug interactions	Medication reconciliation Shared medication audit	Beware interactions between chemotherapy and DXIs No risk of interaction with LMWHs	Prefer LMWH
Comorbidities	Charlson Comorbidity Index [35]	Treatment of comorbidities		No impact on medication choice
Creatinine clearance	Cockcroft formula	Monitoring every 3 months or following acute illness such as infection, dehydration or acute heart failure	If C_{Cr} < 15 mL/min, DXIs and LMWH are both contra-indicated	Prefer LMWH if C_{Cr} 15–30 mL/min

C_{Cr}: creatinine clearance; DXI: direct-acting oral factor Xa inhibitors; LMWH: low-molecular weight heparin; MMSE: Mini-mental state examination.

[a] Low level of evidence.

S. Laporte et al. Archives of Cardiovascular Diseases. 2024; 117:1, 45-59

Quelles données pour les patients thrombopéniques ?

Plaquettes / mm^3	Evènement thromboembolique veineux aigu (< 1 mois)	Evènement thromboembolique veineux non aigu
< 100.000 – 50.000	Pleine dose AOD ou HBPM pleine dose	Pleine dose AOD HBPM pleine dose
< 50.000 – 25.000	HBPM 75 %	HBPM 50 %
< 25.000	HBPM prophylactique et transfusion de plaquettes	

Propositions

Insuffisance rénale

Patients avec insuffisance rénale :

2.5.2. Recommandations de traitement

- Au moment du diagnostic de la CAT, il est recommandé **d'évaluer la fonction rénale** en évaluant le débit de filtration glomérulaire à l'aide d'une formule validée.

- Nous suggérons de **surveiller la fonction rénale tout au long du suivi**, en particulier en cas de lésions rénales aiguës dues à l'EP ou lorsque le patient est traité avec des médicaments dont la toxicité rénale est connue.

- Chez les patients atteints d'insuffisance rénale, nous suggérons d'évaluer et **d'éliminer, si possible, les facteurs de risque hémorragique modifiables**, tels que la co-prescription de médicaments (par exemple des antiplaquettaires) présentant un **risque d'interactions médicamenteuses**.

S. Laporte et al. Archives of Cardiovascular Diseases. 2024; 117:1, 45-59

Propositions

Insuffisance rénale

Patients avec insuffisance rénale :

2.5.2. Recommandations de traitement

…

- Chez les patients présentant une insuffisance rénale légère à modérée (DFGe30-60 ml/min/1,72 m2), nous recommandons de prescrire la **dose thérapeutique complète standard d'HBPM ou de DXI** pour le traitement aigu de la CAT

- Chez les patients dont le DFGe est < 30 ml/min/1,72 m2, nous suggérons d'adapter la stratégie anticoagulante en fonction des besoins:
  - Chez les patients dont le DFGe est compris entre 15 et 30 ml/min/1,72 m2, nous suggérons de prescrire une **HBPM** plutôt qu'un anticoagulant oral (DXI ou AVK).
  - chez les patients avec un DFGe <15 mL/min/1,72 m2, ou sous dialyse, nous suggérons de discuter du choix du traitement avec le néphrologue au cas par cas, parmi les options suivantes : HNF ou AVK.

S. Laporte et al. Archives of Cardiovascular Diseases. 2024; 117:1, 45-59

Propositions

Faible poids corporel

Patients avec faible poids corporel :
2.5.2. Recommandations de traitement

- Nous recommandons l'utilisation d'un anticoagulant à la dose thérapeutique complète standard chez les patients de faible poids corporel en utilisant la **même dose thérapeutique**.
    - les données disponibles ne permettent pas de recommander un DXI plutôt qu'une HBPM ou vice versa chez les patients de faible poids corporel.
    - Nous suggérons d'utiliser l'une ou l'autre de ces classes de médicaments **en fonction du profil de risque global** du patient et de ne pas prendre en compte le faible poids en tant que tel dans le choix du traitement anticoagulant entre les DXI et les HBPM

- Nous suggérons de ne pas suivre les niveaux de pic ou résiduel des DXIs parce que ces données ne peuvent actuellement pas être utilisées pour éclairer les décisions de traitement.

S. Laporte et al. Archives of Cardiovascular Diseases. 2024; 117:1, 45-59

Traitement initial

Propositions

Risque hémorragique :

Table 3
Situations where an LMWH may be preferred over a DXI as initial CAT treatment.

Tumour site	Clinical setting
0esogastric tumour or non-resected colorectal tumour	With anaemia identified by iron deficiency or history of recent bleeding
Non-resected urothelial or gynaecological (especially cervical) cancer	With anaemia identified by iron deficiency or history of recent bleeding
Metastasis of renal carcinoma or melanoma	If appearance on imaging is indicative of a risk of bleeding (hypervascularisation+++)
Primary or secondary location close to large pulmonary vessels	All clinical settings
Inoperable locally advanced breast cancer with skin involvement.	With anaemia identified by iron deficiency or history of recent bleeding
Primary or secondary location of cutaneous tumours or sarcoma	With anaemia identified by iron deficiency or history of recent bleeding

LWMH: low molecular weight heparin; CAT: cancer-associated thromboembolism.
The table illustrates settings where it may be more difficult to stop or control a major or clinically relevant bleed.

Isabelle Mahé et al. Archives of Cardiovascular Diseases,2024;117:1,29-44

Epidemiology of cancer-associated venous thrombosis

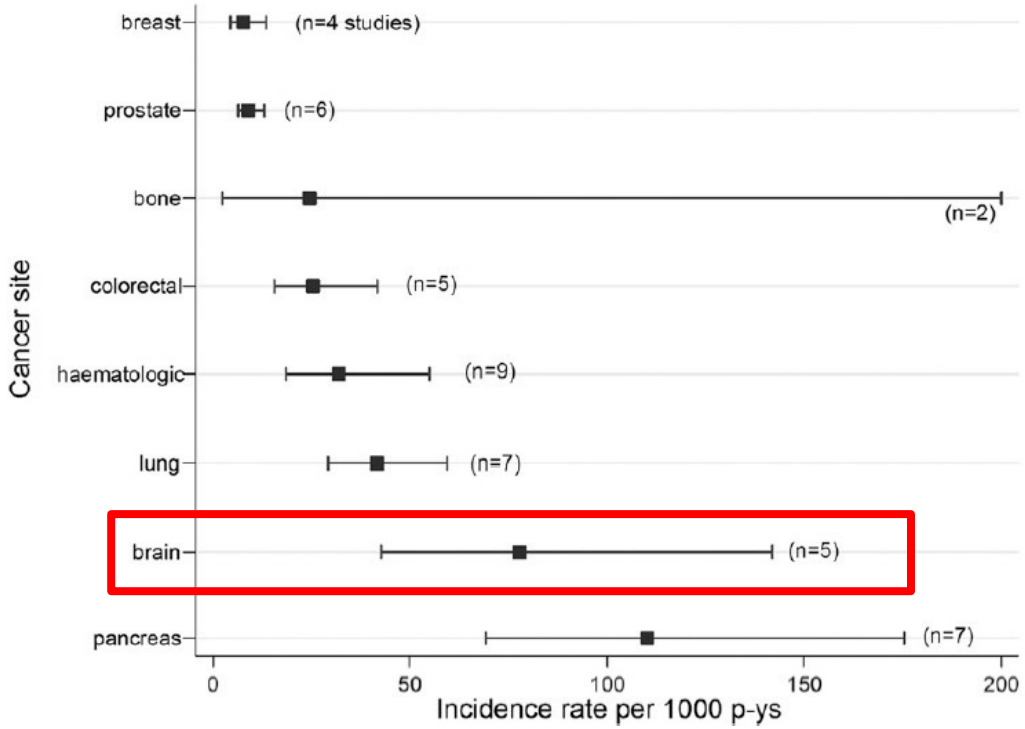
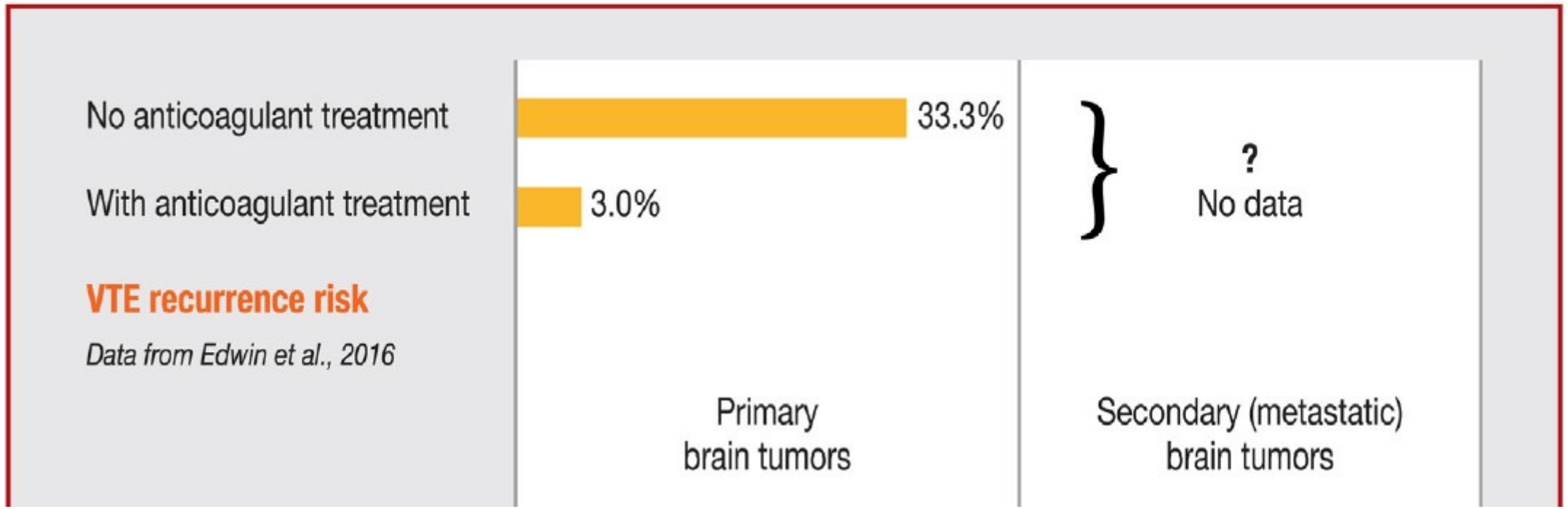


Figure 2. Pooled incidence rates (per 1000 person-years) of venous thrombosis per type of cancer. Only studies with start of follow-up at time of cancer diagnosis were included. Numbers in brackets refer to the number of studies that contributed to the pooled estimate. Figure from Horsted Plos Med 2012.[17]

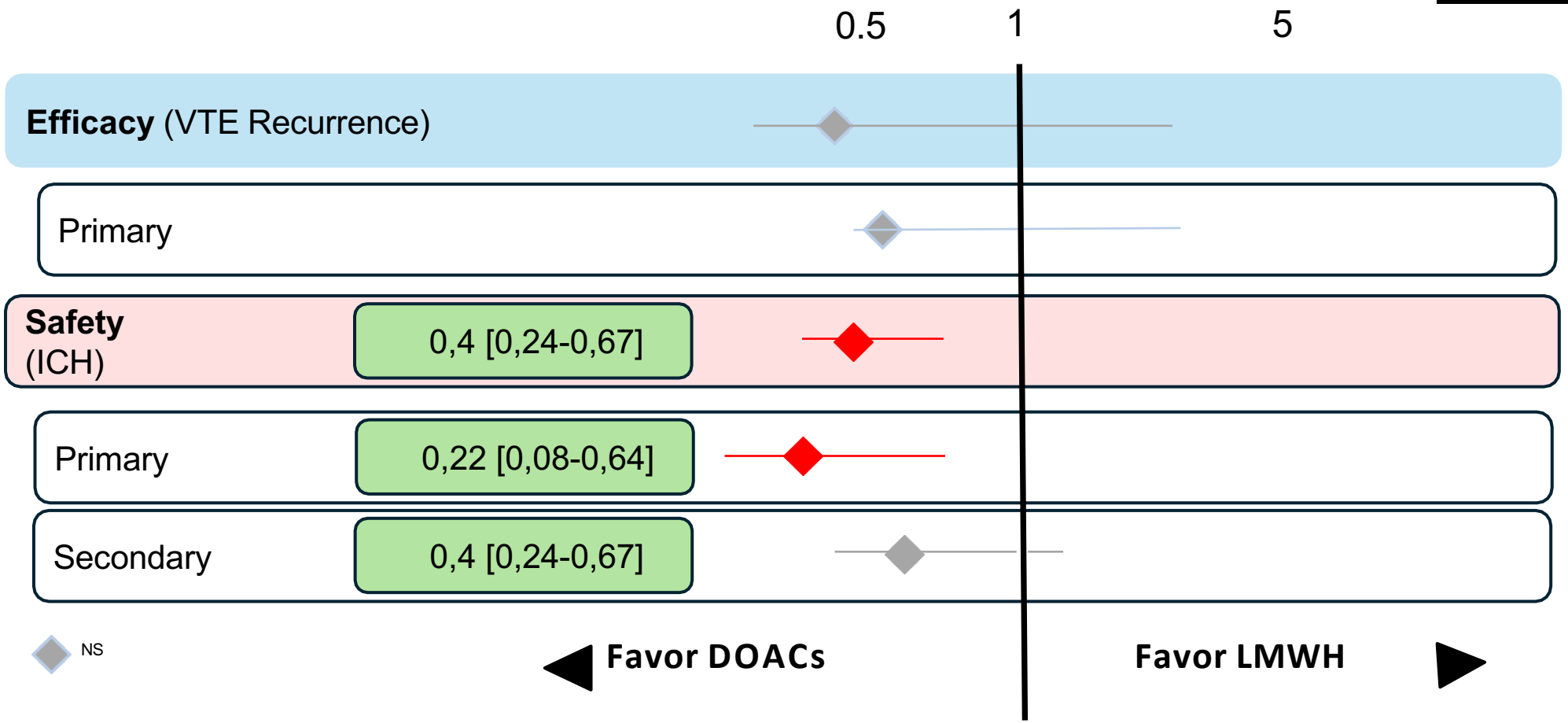
Timp JF, Blood 2013; 122(10):1712-23

In patients untreated with anticoagulants, the rate of VTE recurrence is up to 30% over 2y



- we recommend using an anticoagulant at a full therapeutic dose in patients with primary and secondary brain tumours experiencing a VTE, as in other cancer patients experiencing a VTE. *Expert panel ranking: 3.81 out of 4.00;*

Efficacy / Safety DOACs vs LMWH



Metaanalysis – 6 studies – 655 pts

Frere C, Res Pract Thromb Haemost 2023

- the available data do not permit recommending a DXI over a LMWH or vice versa. We suggest using either of these drug classes in function of the overall risk profile of the patient. *Expert panel ranking: 3.77 out of 4.00;*

- due to the lack of data/evidence with intensive DXI regimens (with loading doses) in the initial phase of CAT, we propose to use LMWH during the first phase of treatment (1 to 3 weeks). *Expert panel ranking: 3.77 out of 4.00;*

7.2. Patients with a bleeding malignant brain tumour

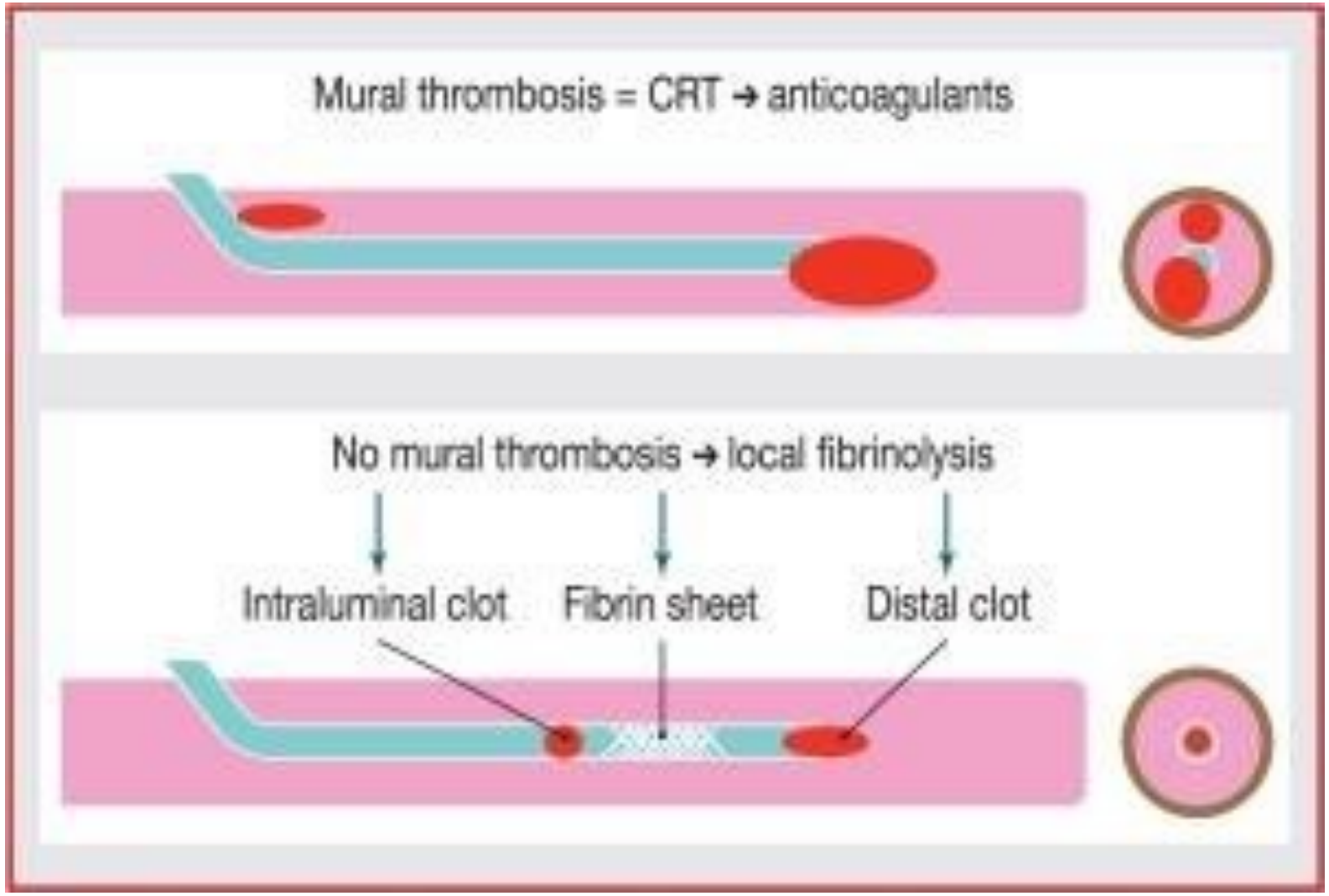
- in case of old bleeds (> 72 h) which are asymptomatic, we propose initiating an anticoagulant at full therapeutic dose,

7.3. Patients receiving bevacizumab

- in patients receiving bevacizumab undergoing a VTE, we recommend initiating an anticoagulant at full dose. *Expert panel ranking: 3.88 out of 4.00;*

7.4. Cerebral radiotherapy

Thrombose veineuse associée à un cathéter veineux central



Elias A, et al. Arch Cardiovasc Dis . 2024 Jan;117(1):72-8

Recommandations Traitements

- **Anticoagulation**

- **Prise en charge initiale:**

- Nous ***suggérons*** une **anticoagulation curative pendant au moins 3 mois** pour les patients cancéreux souffrant d'une CRT symptomatique des veines profondes proximales (y compris les veines brachiales).

- Nous ***suggérons*** d'administrer une **dose curative d'une HBPM ou d'un inhibiteur direct du facteur Xa par voie orale** (avec ou sans dose de charge), tout en respectant toutes les contre-indications de ces anticoagulants.

- **Au-delà des trois premiers mois de traitement anticoagulant:**

- Nous ***suggérons*** de **poursuivre l'anticoagulation tant que le cancer reste actif ou traité et que le cathéter est en place.**

- Nous ***proposons*** les options suivantes :
  - Dose curative d'anticoagulant avec une HBPM ou un inhibiteur du facteur Xa par voie orale.
  - L'arrêt de l'anticoagulation peut être une option dans certains cas (par exemple en cas de risque hémorragique élevé, de résolution complète du thrombus, de cancer qui n'est plus actif ou d'absence de traitement prothrombotique).

Elias A, et al. Arch Cardiovasc Dis . 2024 Jan;117(1):72-8

Recommandations Traitements

- **Retrait du cathéter:**

- Nous ***suggérons*** de **ne pas retirer le cathéter** tant qu'il est **utilisé, fonctionnel, bien positionné** avec une extrémité proximale à la jonction entre l'oreillette droite et la veine cave supérieure, qu'il n'est **pas infecté** et que **l'évolution de la CRT est favorable** sous anticoagulants.

- Pour les patients souffrant d'une CRT, nous ***suggérons*** de **retirer le catheter s'il n'est plus nécessaire**.

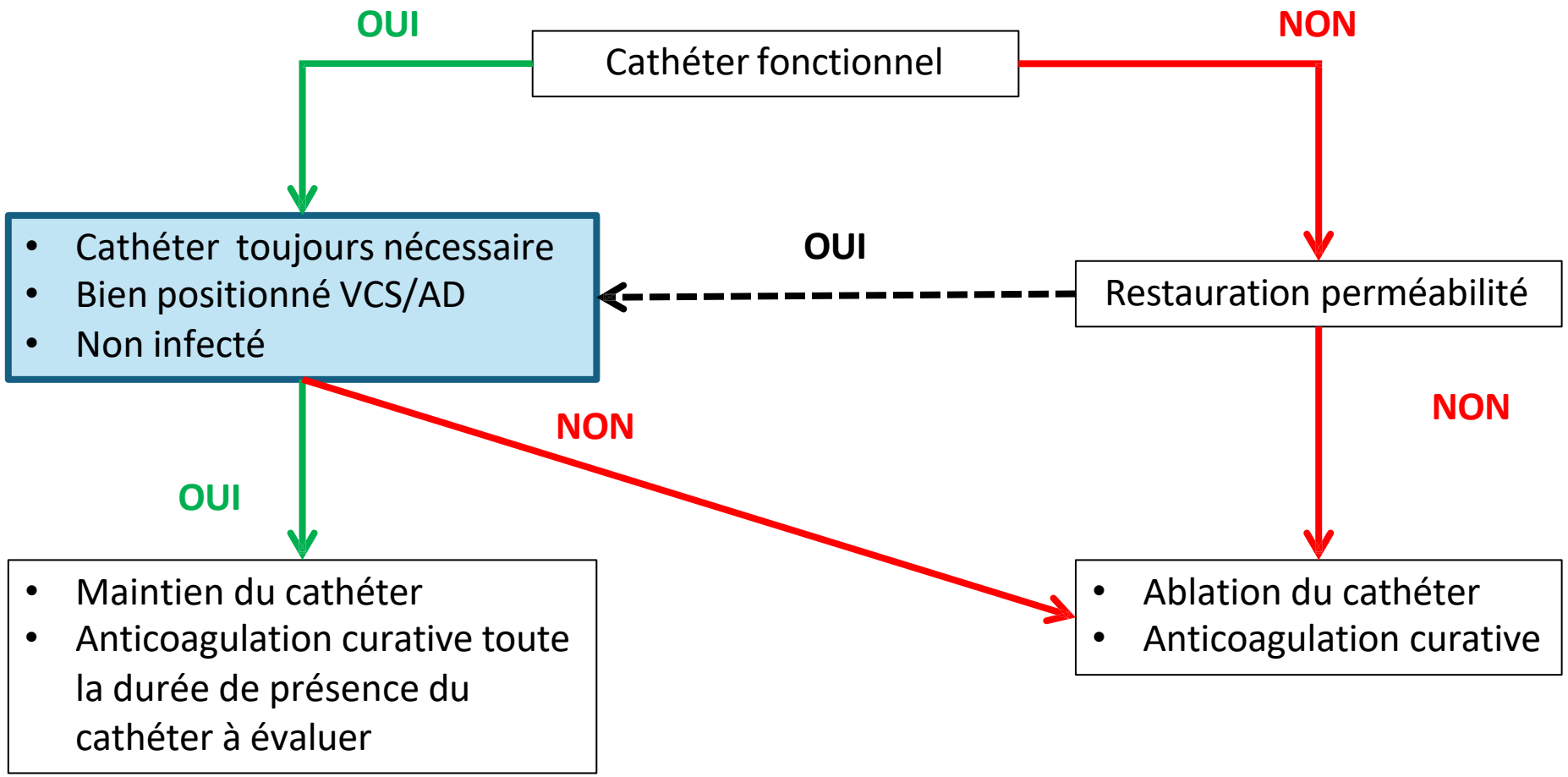
- En l'absence d'infection associée au cathéter, nous ***suggérons*** de retirer le CVC après un **minimum de 2 jours d'anticoagulation curative**.

- Nous ***suggérons*** de poursuivre les anticoagulants pendant **au moins 1 mois après le retrait du cathéter**, avec une durée totale **minimale d'anticoagulation de 3 mois** après le début du traitement anticoagulant.

- En raison d'un risque hémorragique plus élevé, nous ***suggérons*** que la **thrombolyse** soit discutée dans des **centres spécialisés** chez les patients ayant une thrombose volumineuse (par exemple, syndrome cave supérieur) et n'ayant pas de contre-indications à la thrombolyse.

Elias A, et al. Arch Cardiovasc Dis . 2024 Jan;117(1):72-8

Ablation cathéter ?



Récidive d'Embolie Pulmonaire/TVP

- Epidémiologie
  - Fréquence
  - Facteurs de risque
- Diagnostic
  - Clinique, D-dimères, scanner, scintigraphie, E-doppler
  - Pièges…
- Traitement

Archives of Cardiovascular Disease 117 (2024) 84–93

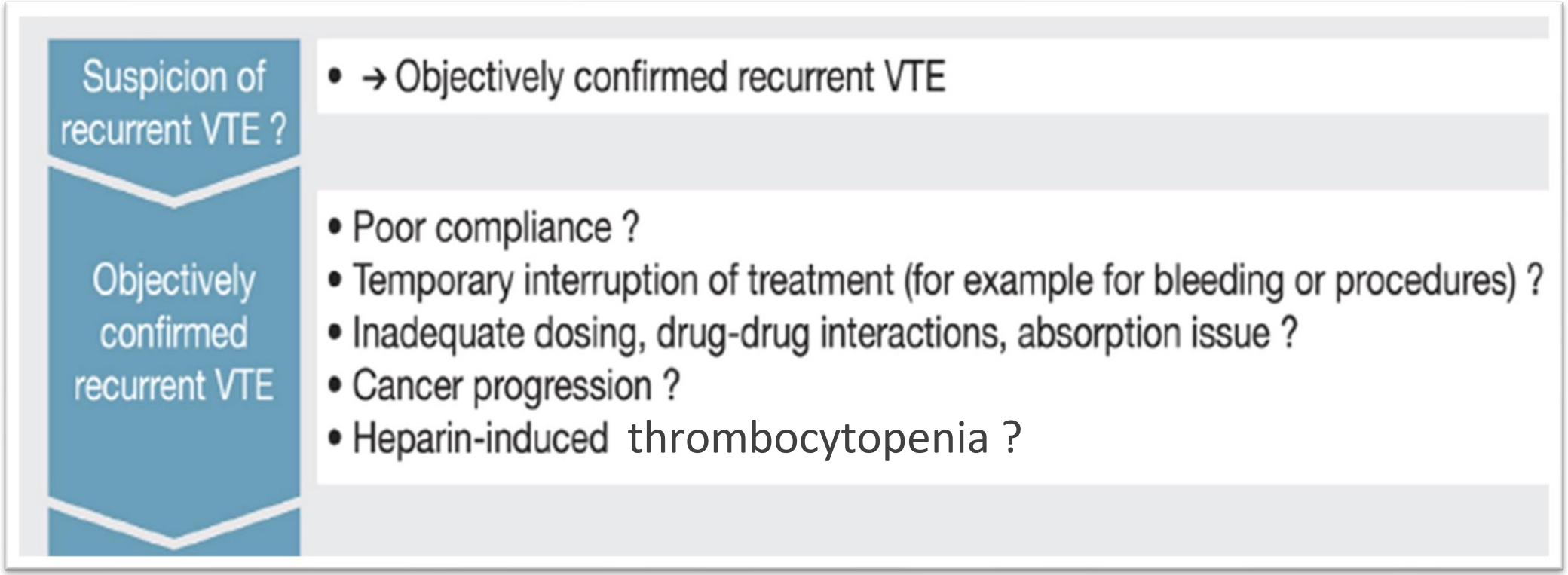
Review

Recurrent venous thromboembolism in anticoagulated cancer patients: Diagnosis and treatment

Laurent Bertoletti[a,j,1,*], Philippe Girard[b,j,1], Antoine Elias[c,j], Olivier Espitia[d], Jeannot Schmidt[e,j], Francis Couturaud[f,j], Isabelle Mahé[g,h,j,2], Olivier Sanchez[h,i,j,2], for the INNOVTE CAT Working Group[3]

Récidive d'EP/TVP : Traitement

1. Questions



Bertoletti, Arch Cardiovasc Dis 117 (2024) 84–93

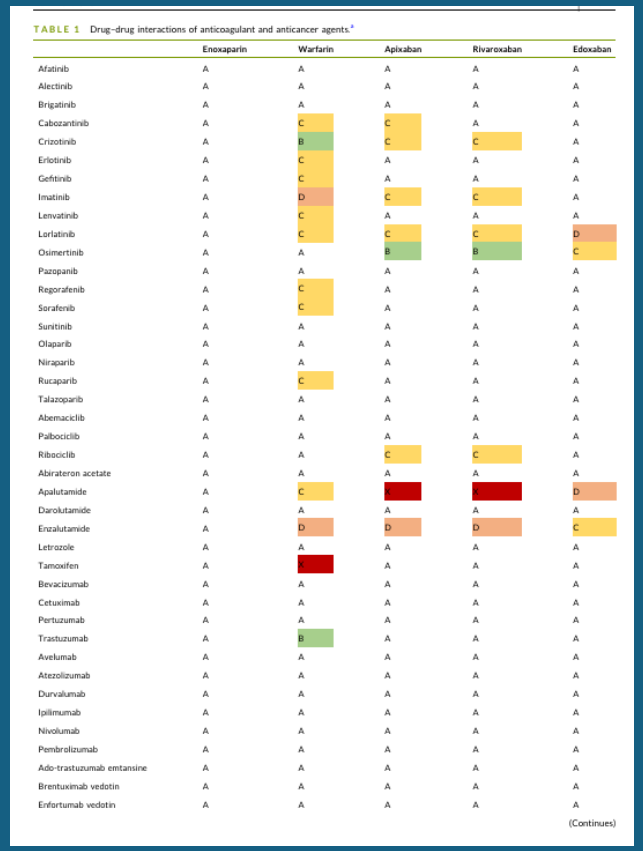


TABLE 1 Drug–drug interactions of anticoagulant and anticancer agents.[a]

	Enoxaparin	Warfarin	Apixaban	Rivaroxaban	Edoxaban
Afatinib	A	A	A	A	A
Alectinib	A	A	A	A	A
Brigatinib	A	A	A	A	A
Cabozantinib	A	C	C	A	A
Crizotinib	A	B	C	C	A
Erlotinib	A	C	A	A	A
Gefitinib	A	C	A	A	A
Imatinib	A	D	C	C	A
Lenvatinib	A	C	A	A	A
Lorlatinib	A	C	C	C	D
Osimertinib	A	A	B	B	C
Pazopanib	A	A	A	A	A
Regorafenib	A	C	A	A	A
Sorafenib	A	C	A	A	A
Sunitinib	A	A	A	A	A
Olaparib	A	A	A	A	A
Niraparib	A	A	A	A	A
Rucaparib	A	C	A	A	A
Talazoparib	A	A	A	A	A
Abemaciclib	A	A	A	A	A
Palbociclib	A	A	A	A	A
Ribociclib	A	A	C	C	A
Abirateron acetate	A	A	A	A	A
Apalutamide	A	C	X	X	D
Darolutamide	A	A	A	A	A
Enzalutamide	A	D	D	D	C
Letrozole	A	A	A	A	A
Tamoxifen	A	X	A	A	A
Bevacizumab	A	A	A	A	A
Cetuximab	A	A	A	A	A
Pertuzumab	A	A	A	A	A
Trastuzumab	A	B	A	A	A
Avelumab	A	A	A	A	A
Atezolizumab	A	A	A	A	A
Durvalumab	A	A	A	A	A
Ipilimumab	A	A	A	A	A
Nivolumab	A	A	A	A	A
Pembrolizumab	A	A	A	A	A
Ado-trastuzumab emtansine	A	A	A	A	A
Brentuximab vedotin	A	A	A	A	A
Enfortumab vedotin	A	A	A	A	A

(Continues)

TABLE 1 (Continued)

	Enoxaparin	Warfarin	Apixaban	Rivaroxaban	Edoxaban
Fam-trastuzumab deruxtecan	A	A	A	A	A
Sacituzumab govitecan	A	A	A	A	A
Bleomycin	A	A	A	A	A
Capecitabin	A	D	A	A	A
Carboplatin	A	B	A	A	A
Cisplatin	A	A	A	A	A
Cyclophosphamide	A	B	A	A	A
Docetaxel	A	A	A	A	A
Doxorubicin	A	A	A	A	A
Etoposide	A	C	A	A	A
Fluorouracil	A	D	A	A	A
Gemcitabine	A	C	A	A	A
Ifosfamide	A	C	A	A	A
Irinotecan	A	A	A	A	A
Oxaliplatin	A	A	A	A	A
Paclitaxel	A	C	A	A	A
Topotecan	A	A	A	A	A

A	No known interactions
B	No action needed
C	Monitor therapy
D	Consider therapy modification
X	Avoid combination

[a]Based on UpToDate Lexicomp drug interactions.

Bolek, Cancer.2023;129:3216–3229

Position of the expert group for assessing and managing potential drug-drug interactions between anticoagulants and anticancer therapies

- We recommend that any combination of anticoagulant and anticancer drug should be investigated for potential drug-drug interactions (DDIs). This search should be extended to any other co-prescribed drugs. *Expert panel ranking: 3.89 out of 4.00*
- Given that discrepancies between databases are sometimes significant, we recommend using multiple sources of information to identify these DDIs, giving preference to regularly updated sources. *Expert panel ranking: 3.57 out of 4.00*
- Concerning the various possible sources of information:
    - We recommend using the information provided in the summary of product characteristics for each molecule prescribed. We suggest to use the DDI thesauri of the registration authorities (ANSM, France [49], British National Formulary [50], fda.gov, USA, ...). *Expert panel ranking: 3.67 out of 4.00*
    - We suggest using one or more databases established by professional associations in onco-cardiology. *Expert panel ranking: 3.67 out of 4.00*
    - We suggest using systematic reviews of the literature by experts in the field, ensuring that they are recently updated. *Expert panel ranking: 3.71 out of 4.00*
    - We suggest using at least one digital database. *Expert panel ranking: 3.64 out of 4.00*
    - We suggest considering a pharmacokinetic DDI to be major if the area under the curve of DXI concentrations is significantly modified by a factor of two. The presence of other pharmacokinetic variability factors (age, body weight and creatinine levels) should be taken into account in the case of a moderate DDI. *Expert panel ranking: 3.58 out of 4.00*
- If no major DDI is identified, the usual recommendations apply. *Expert panel ranking: 3.81 out of 4.00*
- If there is a discrepancy between the different sources used regarding the existence of a major DDI, we suggest that the case be discussed at a multidisciplinary consultation meeting involving an expert pharmacist or pharmacologist. *Expert panel ranking: 3.76 out of 4.00*

Position of the expert group for assessing and managing potential drug-drug interactions between anticoagulants and anticancer therapies

- If a major pharmacodynamic or pharmacokinetic (strong3A4 or P-gp inhibition) DDI is identified with increased DXI concentrations and an increased risk of haemorrhage, we recommend using an LMWH for the initial phase of treatment. After six months of treatment, we recommend assessing the need to continue anticoagulant treatment. If necessary, treatment with LMWH should be continued.

  Alternatively, and after discussion in a multidisciplinary consultation meeting (MCM), a reduced dose of DXI may be suggested in the absence of additional bleeding risk factors such as severe renal or hepatic failure. *Expert panel ranking:3.82 out of 4.00.*

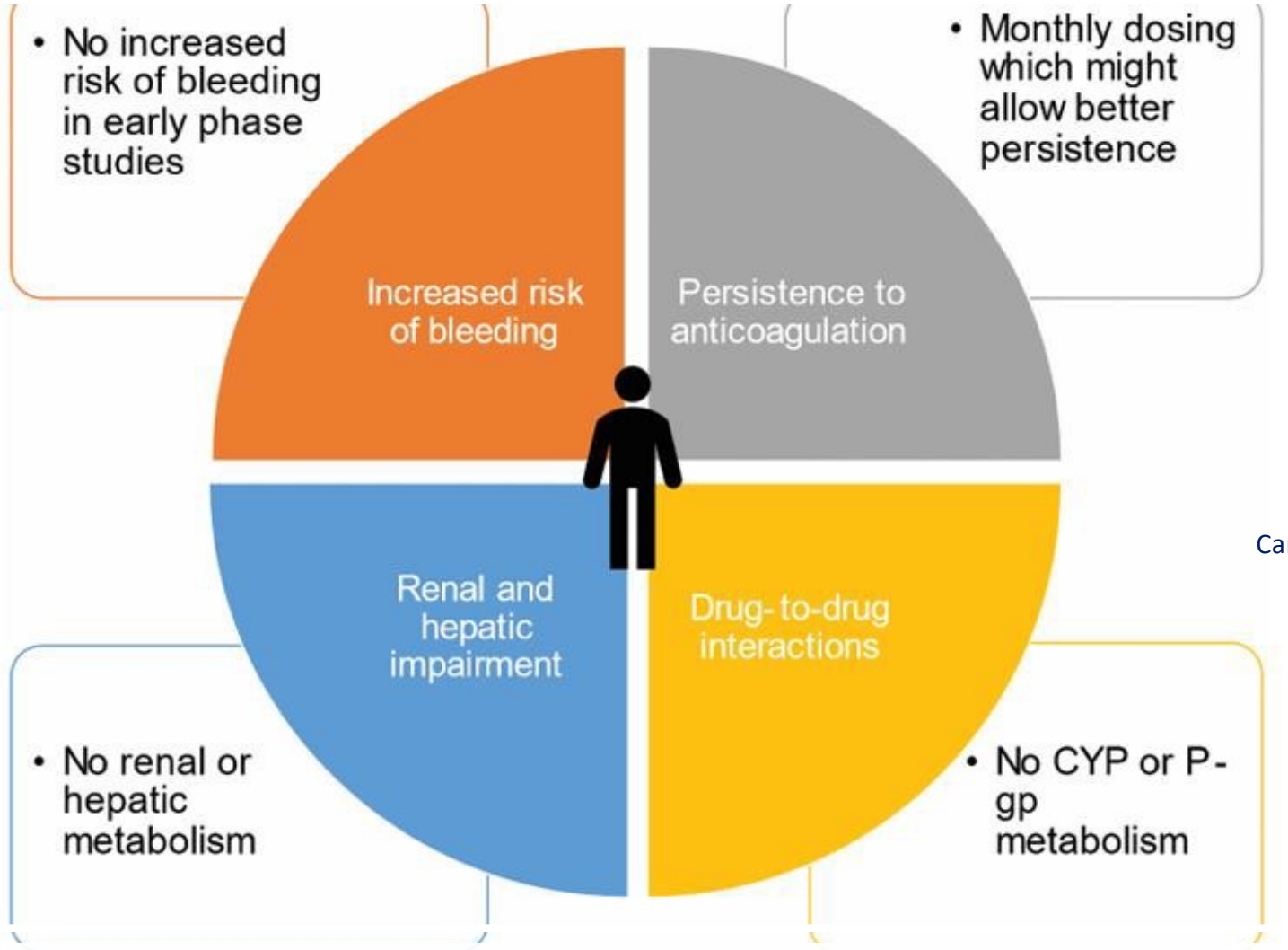
  Alternatively, and after discussion in a MCM, we suggest considering VKAs. *Expert panel ranking: 3.33 out of 4.00*

- If a major pharmacokinetic DDI is identified with reduced DXI concentrations (strong induction of 3A4 and/or P-gp), we recommend using an LMWH for the initial phase of treatment. After six months of treatment, we recommend assessing the need to continue anticoagulant treatment. If necessary, treatment with LMWH should be continued.

  Alternatively, and after discussion with the MCM, a full dose of DXI may be suggested, in the absence of additional thrombotic risk factors. *Expert panel ranking: 3.52 out of 4.00.*

  Alternatively, and after discussion in a MCM, we suggest considering VKAs. *Expert panel ranking: 3.33 out of 4.00*•

- We suggest using edoxaban in cases of induction or strong3A4 inhibition contraindicating the use of rivaroxaban or apixaban. Expert panel ranking: 3.35 out of 4.00
- If a major pharmacokinetic or pharmacodynamic DDI is identified, we recommend giving priority to the anticancer treatment. However, we suggest that the MCM discuss the possibility of an alternative to the current anticancer therapy. Expert panel ranking: 3.79 out of 4.00
- We recommend checking with the patient about any nutritional or health supplements that they may be taking and informing them of any potential interactions with anticoagulants or anticancer drugs. Expert panel ranking: 3.89 out of4.00

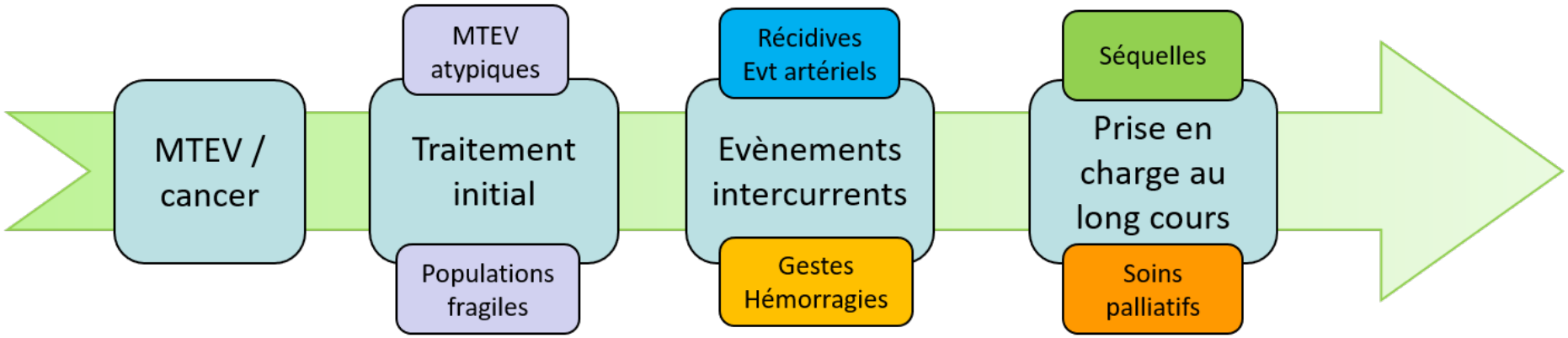


Carrier, The Oncologist, 2023, Vol. 28, No. 7

Lacunes dans les connaissances et besoins non satisfaits liés aux anticoagulants actuels pour la prise en charge des thromboses associées au cancer (centre) et comment les inhibiteurs du facteur XI pourraient résoudre ces problèmes

Parcours de soins de la MTEV/cancer

Médecin Généraliste | Pharmacien | IDE / HAD



Médecine Vasculaire

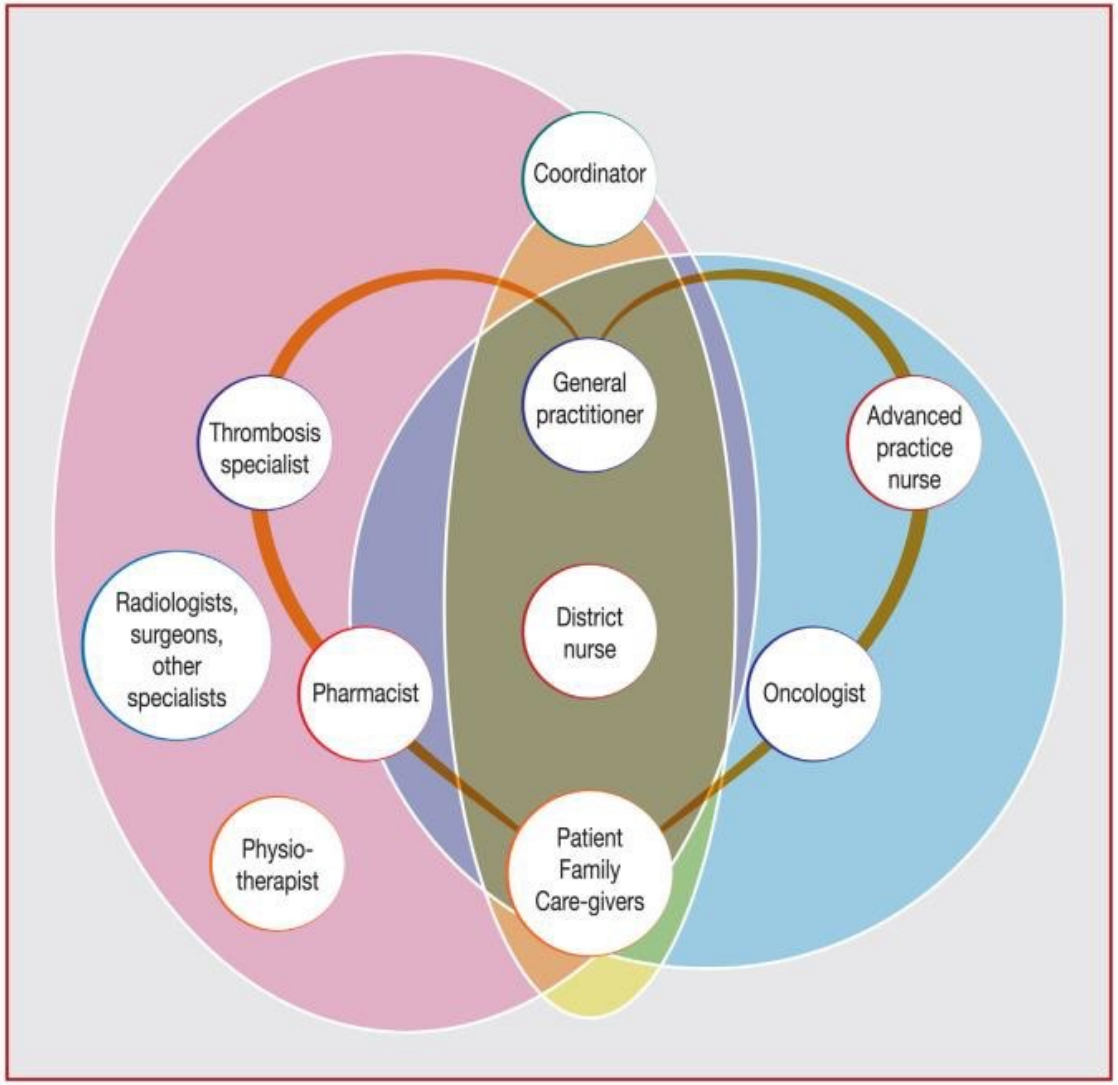
Urgences

Oncologie – pneumologie – cardiologie – médecine interne- neurologie – gériatrie anesthésie- chirurgie- soins de support –, …

Une prise en charge multidisciplinaire

Professionnels de santé impliqués dans la prise en charge des patients atteints de thrombose associée au cancer.

Cercle rose : professionnels de santé impliqués dans les soins de thrombose ;
Cercle bleu : professionnels de santé impliqués dans les soins de cancérologie ;
Zone jaune : soins de proximité quotidiens.



Marie-Antoinette Sevestre et al. Archives of Cardiovascular Diseases, 2024;117:1, 6-15

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