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7th World Congress on Vascular Access

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Current treatment of catheter related thrombosis

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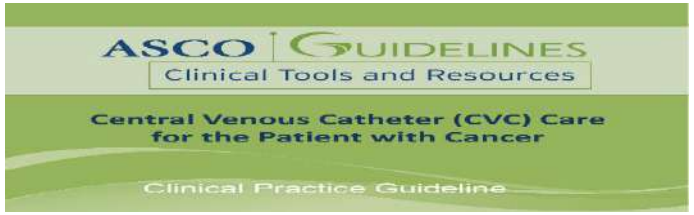
Disclosures

Past Consultancy agreements :
Baxter, B. Braun, Becton Dickinson – Bard, BMR – Brazil
DEKRA, Innova Medica

Present Consultancy agreements :
Chief Medical Officer Plan1Health a Polymedicure Group Co.

WHAT IS NEW ON DVT AND CRT TREATMENT FROM RECENT RELEASED GUIDELINES

-2019 ASCO GUIDELINES
-2019 ITAC GUIDELINES
-2020 NCCN GUIDELINES
-2020 ASH DVT PREVENTION AND TREATMENT GUIDELINES
-2021 ASH GUIDELINES FOR DVT IN CANCER PATIENTS



ITAC CME
International Initiative on Thrombosis and Cancer

NCCN National Comprehensive Cancer Network®
National Comprehensive Cancer Network

American Society of Hematology
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PRELIMINARY CONSIDERATIONS

TREATMENT RECOMMENDATIONS AND THERAPEUTIC LANDSCAPE FOR CATHETER RELATED THROMBOSIS ARE SIMILAR TO THESE FOR DVT OF THE LOWER EXTREMITIES

THERE ARE RELEVANT CHANGES ON DVT TREATMENT FROM RECENT RELEASED GUIDELINES

CR-Thrombosis
GOALS OF THE TREATMENT

- Improve acute symptoms
- Decrease long term morbidity
- Prevent VTE recurrence and/or PE
- Prolonged patency and survival of the catheter unless it is no longer necessary, not functional, dislodged or infected

Maintain the catheter unless no longer needed, non functional, dislodged or infected

- **Even if the line is removed prophylactic anticoagulation is still required to prevent recurrent VTE or PE**
- **A reinsertion of another CVC is often necessary, in particular for cancer patients and DIVA patients**
- **There is no evidence that removal of the catheter improves outcome (ISTH 2013, ACCP 2016, ASH 2020 Guidelines and Recommendations)**

Maintain the catheter unless no longer needed, not functional, dislodged or infected

- ASH 2021 Guideline

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Recommendation 29

For patients with cancer with CVC-related VTE receiving anticoagulant treatment, the ASH guideline panel *suggests* keeping the CVC over removing the CVC (conditional recommendation, very low certainty in the evidence of effects ⊕◯◯◯).

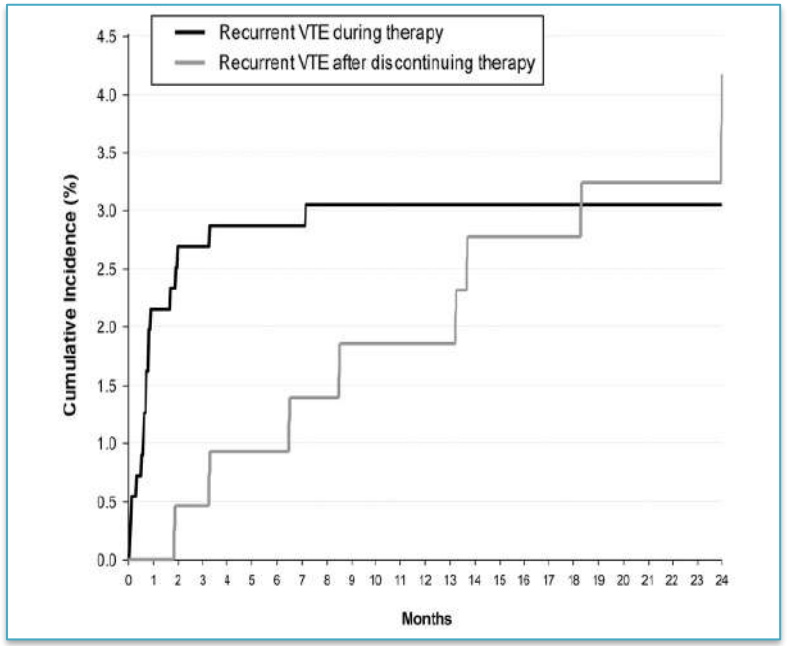
Remarks: If a VTE develops and the CVC is left in place, anti-

12 MONTHS RECURRENT PE AND MORTALITY AFTER CRT

A RIETE registry analysis of recurrent thromboembolism and hemorrhage in patients with catheter-related thrombosis

Lisa Baumann Kreuziger, MD, MS,[a] Lauren Cote, RN, BSN,[b] Peter Verhamme, MD, PhD,[c] Steven Greenberg, MD,[d] Joseph Caprini, MD, MS,[e,f] Francisco José Muñoz, MD,[g] Reina Valle, MD, PhD,[h] and Manuel Monreal Bosch, MD, PhD,[i] for the RIETE Investigators, *Milwaukee, Wisc; Chicago and Evanston, Ill; Leuven, Belgium; and Barcelona and Cantabria, Spain*

JOURNAL OF VASCULAR SURGERY: VENOUS AND LYMPHATIC DISORDERS
July 2015



GLOBAL RECURRENT DVT	**2.58%**
GLOBAL RECURRENT PE	**1.97%**
MORTALITY FOR RECURRENT PE	**0.89%**

VERY LOW ESTMATED RISK OF PE RELATED MORTALITY AFTER CVC INSERTION

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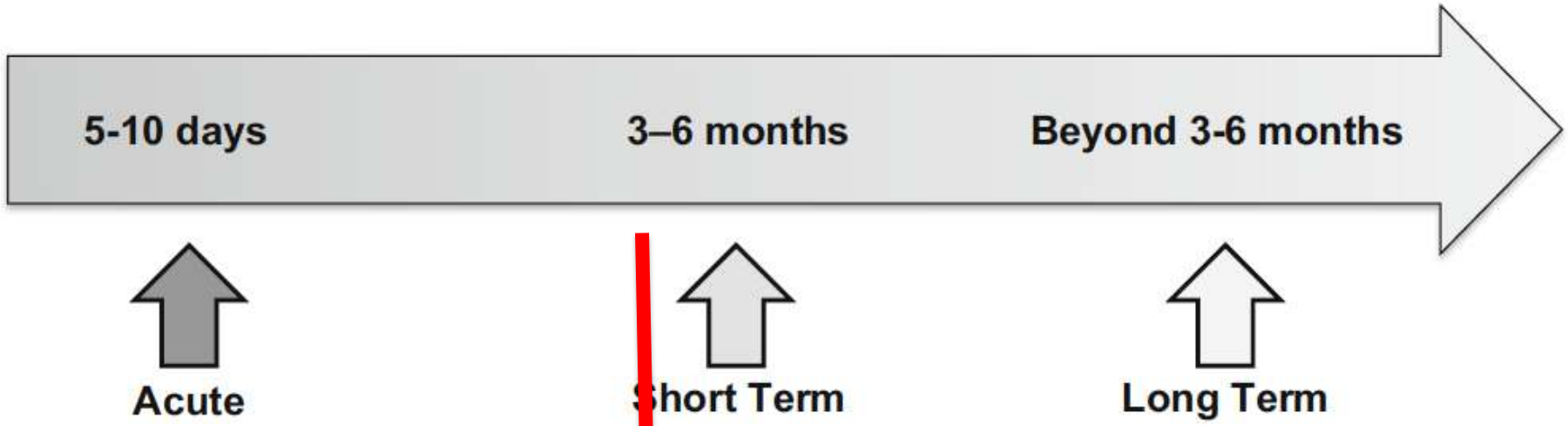
CRT TREATMENT
Technically simple, highly successful and safe

Therapeutic landscape is similar to that of VTE mainly based on anticoagulation obtained by

1. **UFH (patients with severe renal failure)**
2. **LWMH/ Fundaparinux**
3. **VK antagonists**
4. **DOACs (anti-Xa or thrombin inhibitors)**
5. **Thrombolysis (r-TPA)**

THE DIFFERENT PHASES OF CRT TREATMENT

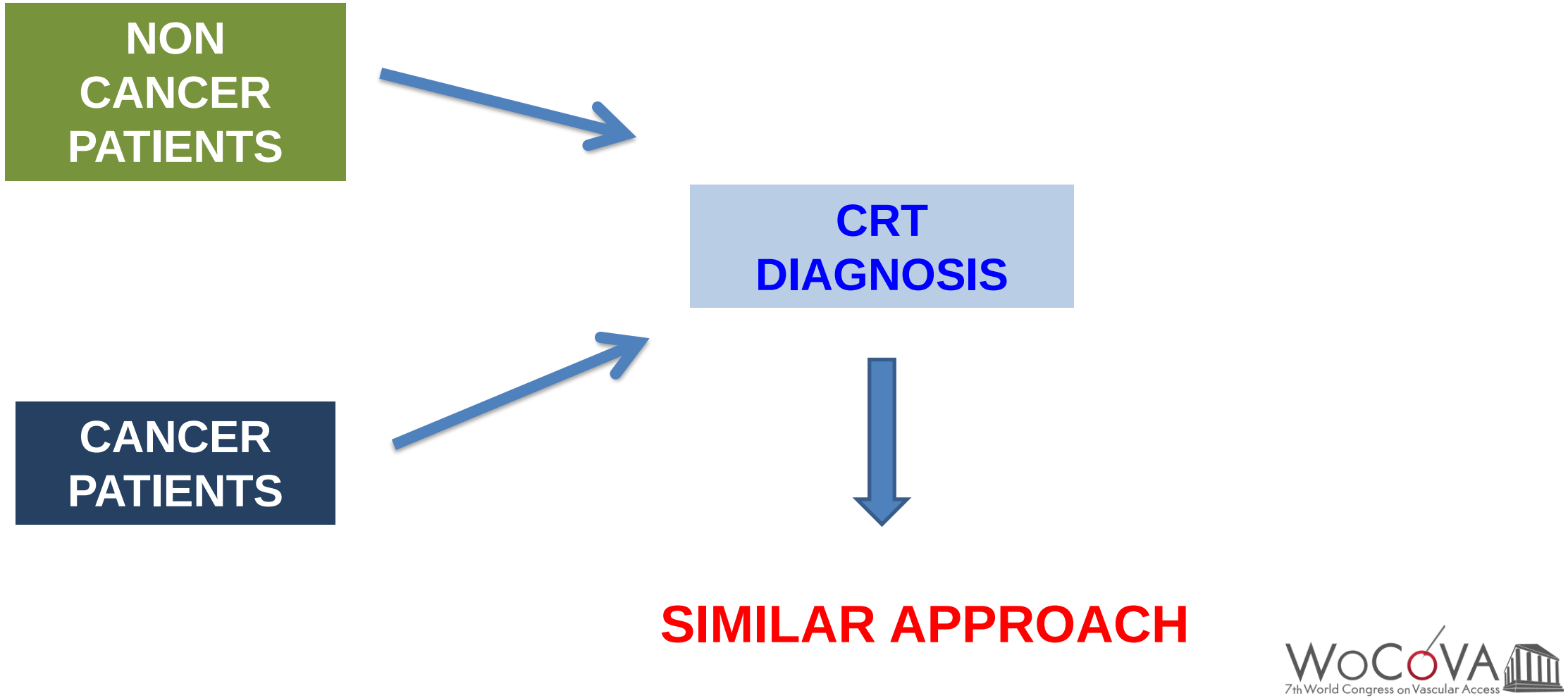


INITIAL PHASE

Until the release of symptoms or the normalization of US or CT imaging

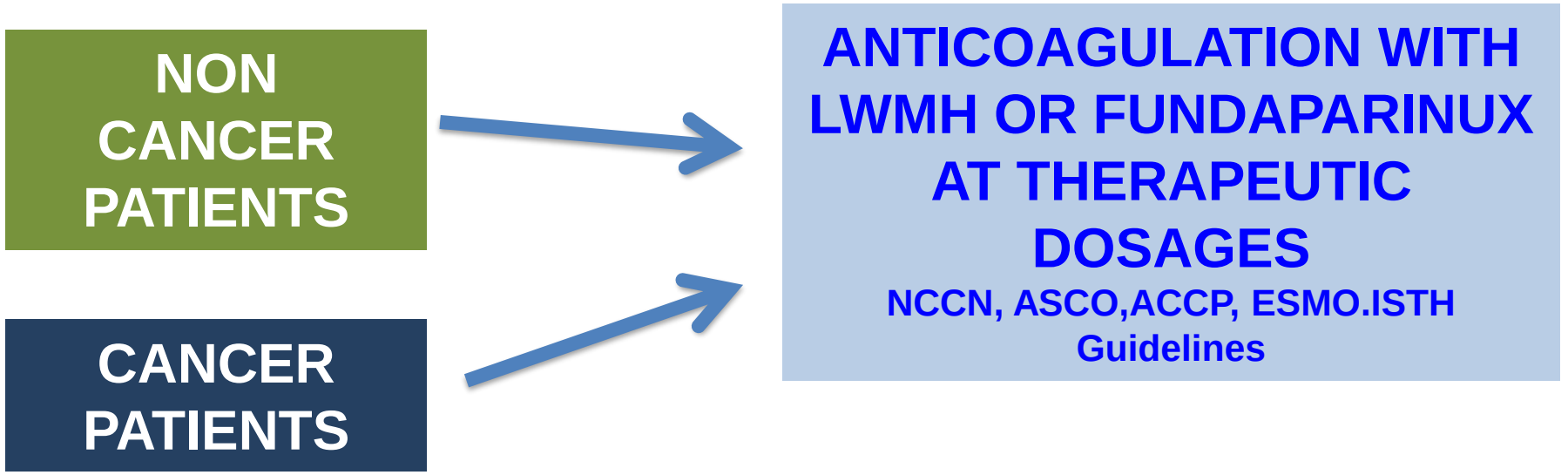
EXTENDED OR INDEFINITE PHASE

PATIENT'S RELATED APPROACH FOR CRT TREATMENT



MANAGEMENT OF CRT
Classic standardized treatment

INITIAL PHASE : from CRT diagnosis until 3 months or resolution of symptoms



For patients with unpaired renal function (Cr Cl < 30 ml/min) and elevated risk of bleeding consider LWMH dose reduction or UFH i.v. infusion APP-dose adjusted

RECOMMENDATIONS FROM RECENT GUIDELINES
INITIAL PHASE TREATMENT

OVERALL PATIENTS WITH CRT and/or VTE

- **DOACs vs Fundaparinux vs LWMH vs VKA**

- One DOAC similar to another DOAC (except for cancer patients)
- Home treatment vs hospital treatment
- Shorter course up to 6 m vs longer (12-24 m) course of primary treatment

RECOMMENDATIONS FROM ASH 2021 GUIDELINES
INITIAL PHASE - MANAGEMENT

CANCER PATIENTS Disease-free or non metastatic

- **DOACs vs Fundaparinux vs LWMH vs VKA**
- **Apixaban or Rivaroxaban or Edoxaban suggested**

- **Short 6 m vs long 12-24 m course treatment**

RECOMMENDATIONS FROM ASH 2021 GUIDELINES
INITIAL PHASE - MANAGEMENT

CANCER PATIENTS Advanced metastatic disease and elevated risk for bleeding

- **LWMH vs DOACs vs VKA**
- **Apixaban or Rivaroxaban or Edoxaban suggested DOACs**

- **Short 6 months vs long 12-24 months course treatment**

LWMH – FUNDAPARNUX DOSAGESFOR FOR CRT TREATMENT

	DOSE SUGGESTED
ENOXAPARIN	1mg/kgb b.i.d 1.5 mg/kg o.d.
DALTEPARIN	100 U/kg b.i.d. 200 U /kg o.d.
NADROPARIN	2850-7600 IU b.i.d. Body weight adjusted
TINZAPARIN	175 U/Kg o.d.
FUNDAPARINUX	5-10 mg o.d. Body weight adjusted

DOACs DOSAGES FOR THE MANAGEMENT OF CRT

INITIAL PHASE: DOACs options

DOAC	VTE treatment	VTE primary prophylaxis
DABIGATRAN	Parenteral anticoagulation for 5 to 10 days; then dabigatran 150 mg twice daily	110 mg for the first day, then 220 mg once daily
APIXABAN	10 mg twice daily for one week, then 5 mg twice daily	2.5 mg twice daily
BETRIXABAN	NOT FDA APROVED FOR TREATMENT	160 mg on the first day, followed by 80 mg once daily, with food
EDOXABAN	Parenteral anticoagulation for 5 to 10 days; then edoxaban 60 mg once daily	NO TRIALS AVAILABLE
RIVAROXABAN	15 mg twice daily with food for three weeks; then 20 mg once daily with food	10 mg once daily, with or without food

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THROMBOLYSIS MANAGEMENT OF CRT

INITIAL PHASE: a marginal role for thrombolysis

- **SVC Syndrome**
- **Acute limb threat**
- **Severe symptoms progression**

Consider r-TPA or urokinase for low bleeding risk patients

CONTINUE ANTICOAGULATION WITH DOACs or LWMH

MANAGEMENT OF CRT

EXTENDED PHASE OF TREATMENT

NON CANCER PATIENTS

- **ANY DOAC over LWMH over VKA over ASA**
- **In case of recurrent VTE under DOACs overlap to Fundaparinux or LWMH**
- **VKA or LWMH in case of CKD stage 3 or >**

For a minimum of 3 months
No need for prolonged treatment in absence of risk factors but consider the persistence of any CVC in place as a risk factor

ALGORYTHM FOR THE MANAGEMENT OF CRT

EXTENDED PHASE OF TREATMENT

CANCER PATIENTS

(NCCN, ASCO,ESMO,ACCP Guidelines)

Indefinite anticoagulation as long as a CVC is in place, active cancer or chemotherapy

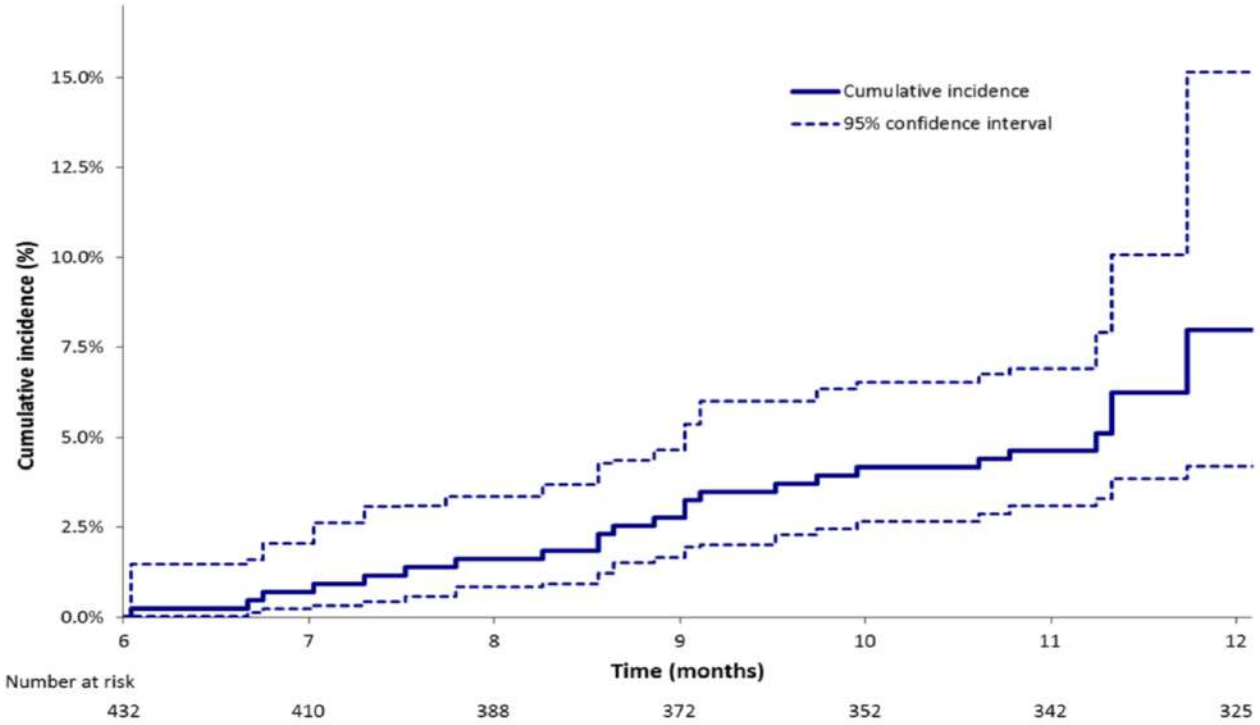
- **DOACs and LWMH or Fundaparinux with a prophylactic dosage**
- **Indefinite anticoagulation as long as a CVC is in place, active cancer under chemotherapy, and other possible risk factors for VTE**
- **Consider no treatment only for disease free patients without risk factors**

RRATES OF RECURRENT VTE IN CANCER PATIENTS

Long-Term Treatment of Cancer-Associated Thrombosis (CAT) Beyond 6 Months in the Medical Practice: USCAT, a 432-Patient Retrospective Non-Interventional Study

Isabelle Mahé [1,2,3,*], Ludovic Plaisance [1], Céline Chapelle [4,5], Silvy Laporte [2,4,5], Benjamin Planquette [2,3,6], Laurent Bertoletti [2,4,5,7,8,9], Francis Couturaud [2,10], Nicolas Falvo [2,11], Lionel Falchero [12], Isild Mahé [1], Hélène Helfer [1,3], Jean Chidiac [1] and Guy Meyer [2,6]

Cancers **2020**, *12*, 2256; doi:10.3390/cancers12082256



OVERALL 5.7% RISK OF RECURRENCE FOR PATIENTS WITH ACTIVE CANCER AND PERSISTENCE OF RISK FACTORS

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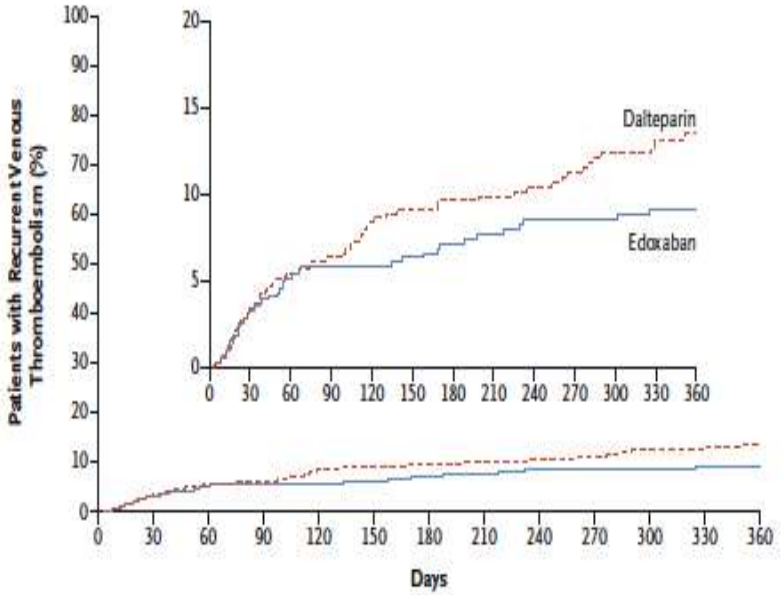
DOACs FOR EXTENDED TREATMENT IN CANCER PATIENTS

EDOXABAN FOR THE TREATMENT OF CANCER ASSOCIATED VTEP ; ROBE TRIAL from HOKUSAI VTE Cancer Investigators

G.E. Raskob, N. van Es, P. Verhamme, et al., N ENGL J MED 2018: 378;615-24

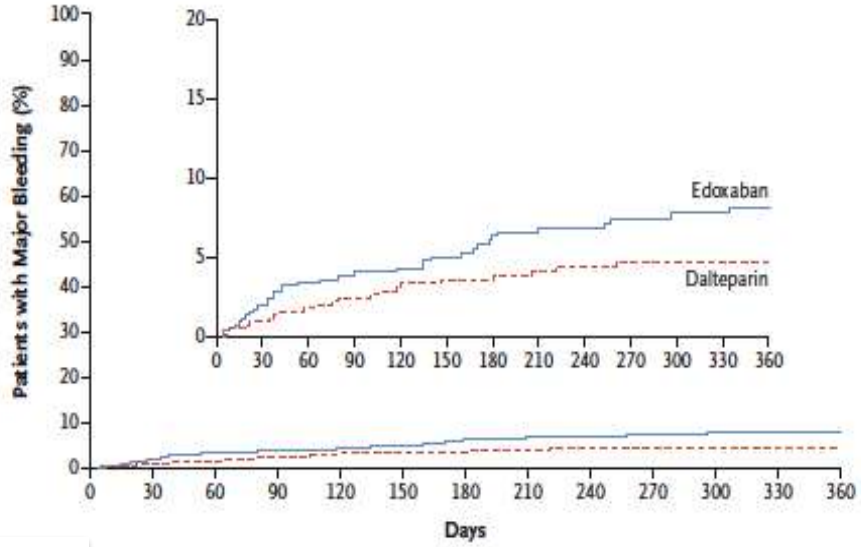
HOKUSAI Trial

RECURRENT VTE



MAJOR BLEEDING

* Major bleeding only for GI tract advanced cancer patients



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DOACs FOR EXTENDED TREATMENT OF CANCER PATIENTS

VOLUME 36 · NUMBER 20 · JULY 10, 2018
JOURNAL OF CLINICAL ONCOLOGY RAPID COMMUNICATION

SELECT-D Trial

Comparison of an Oral Factor Xa Inhibitor With Low Molecular Weight Heparin in Patients With Cancer With Venous Thromboembolism: Results of a Randomized Trial (SELECT-D)

Annie M. Young, Andrea Marshall, Jenny Thirlwall, Oliver Chapman, Anand Lokare, Catherine Hill, Danielle Hale, Janet A. Dunn, Gary H. Lyman, Charles Hutchinson, Peter MacCallum, Ajay Kakkar, F.D. Richard Hobbs, Stavros Petrou, Jeremy Dale, Christopher J. Poole, Anthony Maraveyas, and Mark Levine

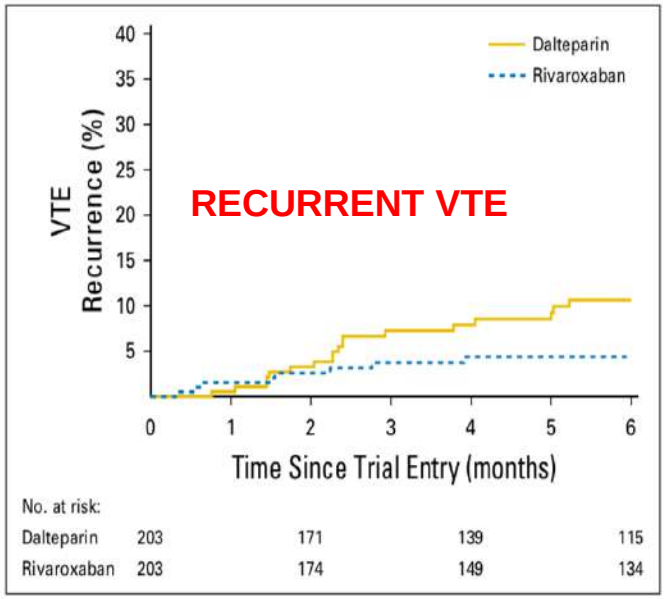

Fig 2. Time to venous thromboembolism (VTE) recurrence within 6 months.

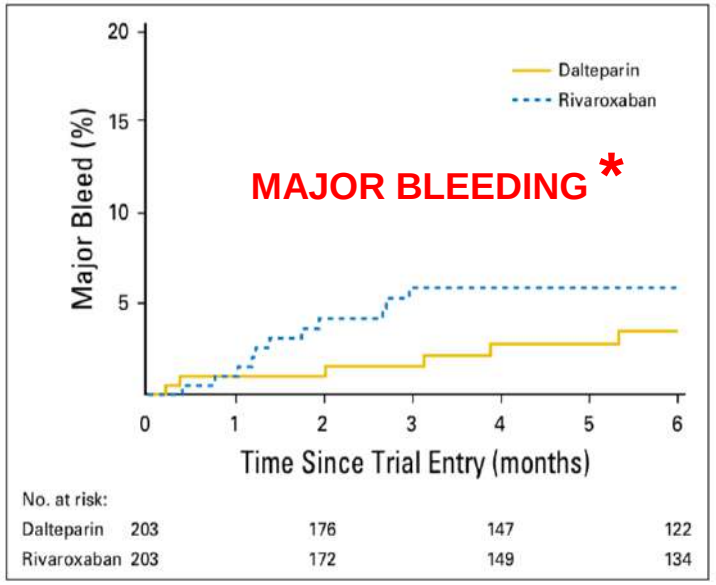

Fig 3. Time to major bleed within 6 months.

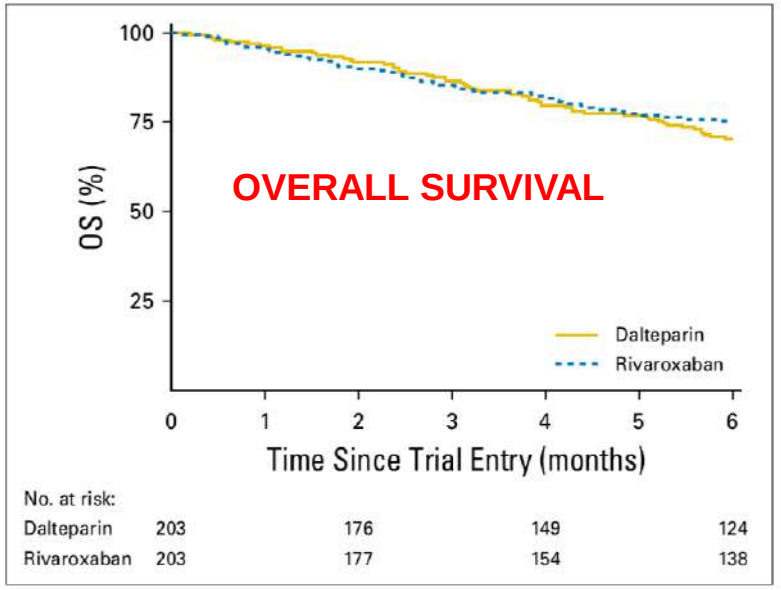

Fig A2. Overall survival (OS) within 6 months.

* Major bleeding only for GI tract advanced cancer patiernts

CHALLENGING SCENARIOS FOR ANTICOAGULATION IN THE CRT TREATMENT

THROMBOCYTOPENIA

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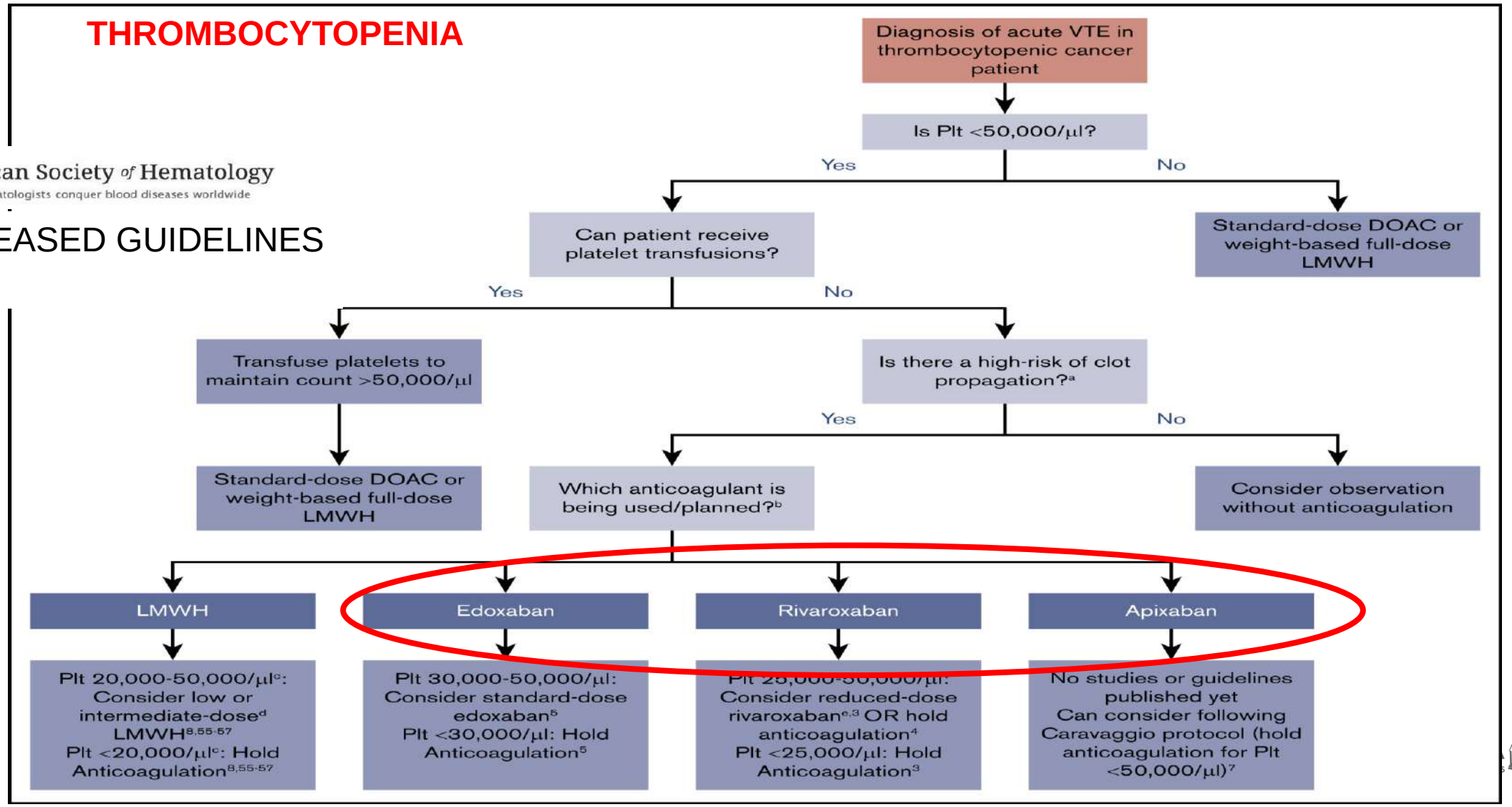
2019 RELEASED GUIDELINES



CHALLENGING SCENARIOS FOR ANTICOAGULATION IN THE CRT TREATMENT

RENAL FAILURE AND LWMH/FUNDAPARINUX

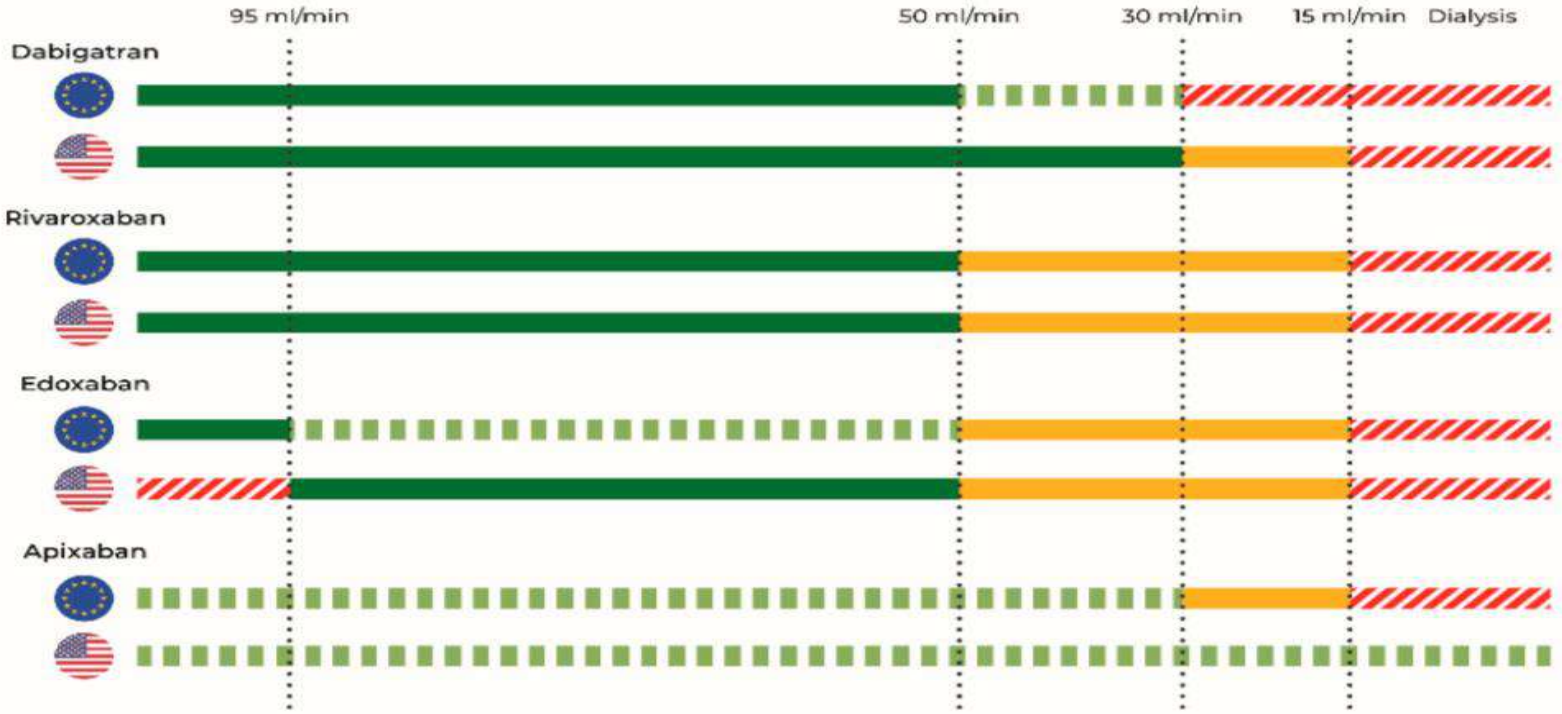
DRUG	Cr CL >30 mL/min	Cr CL less than 30 ml/min
ENOXAPARIN	1mg/Kg BID	1mg/Kg OD
DALTEPARIN	200 IU/Kg OD	No reduction except for low antiXa levels
NADRPOARIN	2850-7600 IU BID Body weight adjusted	50 % dose reduction OD
TINZAPARIN	175 U/Kg OD	No reduction except for low antiXa levels
FUNDAPARINUX	5-10 mg OD Body weight adjusted	NOT INDICATED

CHALLENGING SCENARIOS FOR ANTICOAGULATION IN THE CRT TREATMENT

CKD AND DOACs RENAL CLEARANCE

- RIVAROXABAN 23% 
- APIXABAN 27% 
- EDOXABAN 50% 
- DABIGATRAN 80% 

DOACs dose adjustment in CKD



Standard dose
- dabigatran 150 mg BID
- rivaroxaban 20 mg OD
- edoxaban 60 mg OD
- apixaban 5 mg BID

Reduced dose
- dabigatran 110 mg BID (EU) or 75 mg BID (US)
- rivaroxaban 15 mg OD
- edoxaban 30 mg OD
- apixaban 2.5 mg BID

Standard or reduced dose
Dose reduction criteria:
- dabigatran: high bleeding risk
- edoxaban: weight ≤ 60 kg or concomitant potent P-Gp inhibitor
- apixaban: at least 2 criteria among age ≥ 80 years, weight ≤ 60 kg, creatinine ≥ 1.5 mg/dl

Contraindicated

TIMING FOR CATHETER REMOVAL (if necessary) AFTER CRT DIAGNOSIS AND ANTICOAGULATION TREATMENT

CRT DIAGNOSIS → **CATHETER RETRIVAL**

3-7 DAYS ANTICOAGULATION

EXTENDED 3 MONTS ANTICOAGULATION IF RISK FACTORS AT PROPHYLACTIC DOSAGES

Optimal Timing for Removal of an Upper Extremity Central Catheter When Associated with a Deep Vein Thrombosis: A Venous Thromboembolism Network US Multicenter Retrospective Cohort Study

Damon E. Houghton, et al *Blood* (2019) 134 (Supplement 1): 325.

Table 2: Outcomes of pulmonary emboli (PE) and death within 7 days by treatment group

	N	PE within 7 days N (%)	P value	PE or death within 7 days N (%)	P value
Delayed or No Removal	200	1 (0.5)	1.0	3 (1.5)	0.68
Early Removal (<48hrs)	312	2 (0.64)		3 (1)	
Removal Only	119	0		3 (2.5)	

Anticoagulation

No treatment

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CRT TREATMENT UPDATES FROM RECENT GUIDELINES

ANTICOAGULATION IS ALWAYS ESSENTIAL

1 IMPLEMENTED USE OF DOACs

- One DOAC similar to another DOAC
- For Cancer Patients better use Apixaban and Rivaroxaban

2 EXTENDED TREATMENT CAN BE REDUCED TO 3 MONTHS FOR THE MAJORITY OF PATIENTS

- Reduction not suggested for active cancer patients , CT or persistence of risk factors or a CVC in place.

3 LIMITED USE OF INDEFINITE TREATMENT

- Applicable for persistence of risk factors, active cancer patients , or a CVC in place

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