Cremona 10 marzo 2017

Terapia e durata del trattamento

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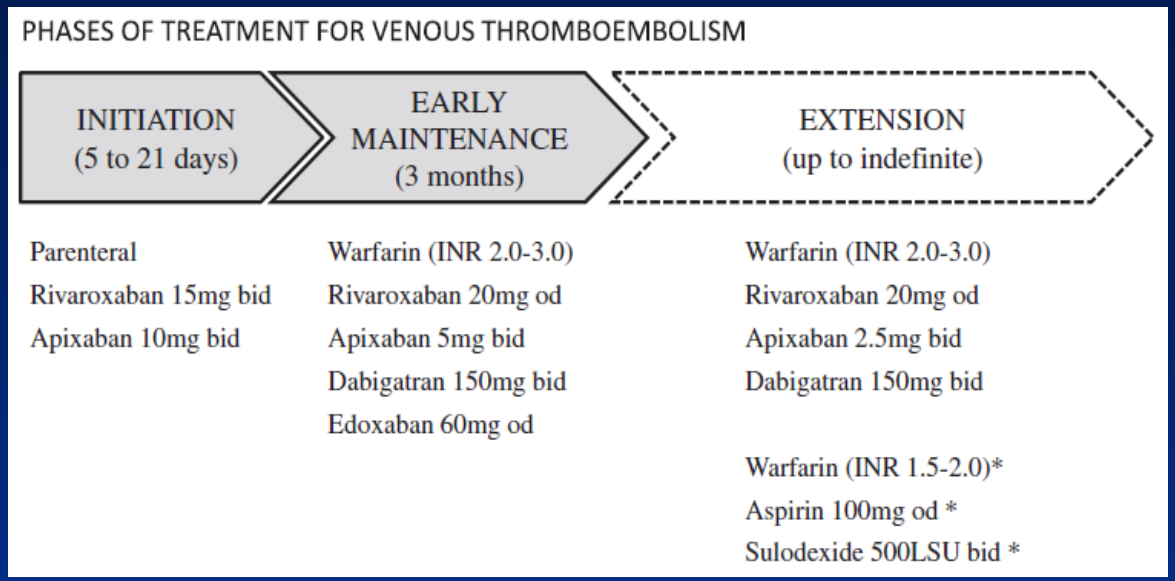
From Blondon & Bounameaux, Circulation 2015



Initial → Long-Term → Extended

From Kearon et al., Chest 2016

Terapia iniziale e lungo-termine TEV: Importanti differenze tra i NAO

- Terapia parenterale per i primi 5-9 gg poi NAO
  - dabigatran (Pradaxa) 150 mg BID
  - edoxaban (Lixiana) 60 mg OID
- Subito NAO
  - rivaroxaban (Xarelto) 15 mg BID x 21 gg poi 20 mg OID
  - apixaban (Eliquis) 10 mg BID x 7 gg poi 5 mg BID

Recurrence incidence rates since the beginnig of therapy for VTE

- At 14 d. = 55.4 per 100 person-years
- 90 d. = 30.0
- 180 d. = 17.7

The rate of VTE recurrence is highest during heparin therapy and the transition to warfarin.

The 2-week case fatality rates for recurrent PE and recurrent DVT alone are 11% and 2%, respectively (Heit et al. Blood 2011)

START–Register

SURVEY ON ANTICOAGULATED PATIENTS – REGISTER

Registro computerizzato per la raccolta dei dati di pazienti trattati cronicamente con anticoagulanti

Percentuale del tempo trascorso sotto, entro o sopra il range terapeutico nei primi tre mesi di trattamento in relazione alle classi di score

Score	N. of patients (%)	Percentage of time below TR	Percentage of time within TR (TTR)	Percentage of time above TR
Score Groups				
0-1	916 (70%)	31±26.7	61±26	8.4±14
≥ 2	392 (30%)	39±28	53±26	7.7±13.7
P value		p= 0.0001	p= 0.0001	p= 0.61

Palareti et al., Thromb Haemost 2016

NAO: Prevedibile migliore qualità nella fase iniziale del trattamento del TEV

L’iniziale fase di terapia con LMWH+warfarin è particolarmente difficile da regolare

Terapia per la “maintenance”: primi 3-6 mesi

AVK

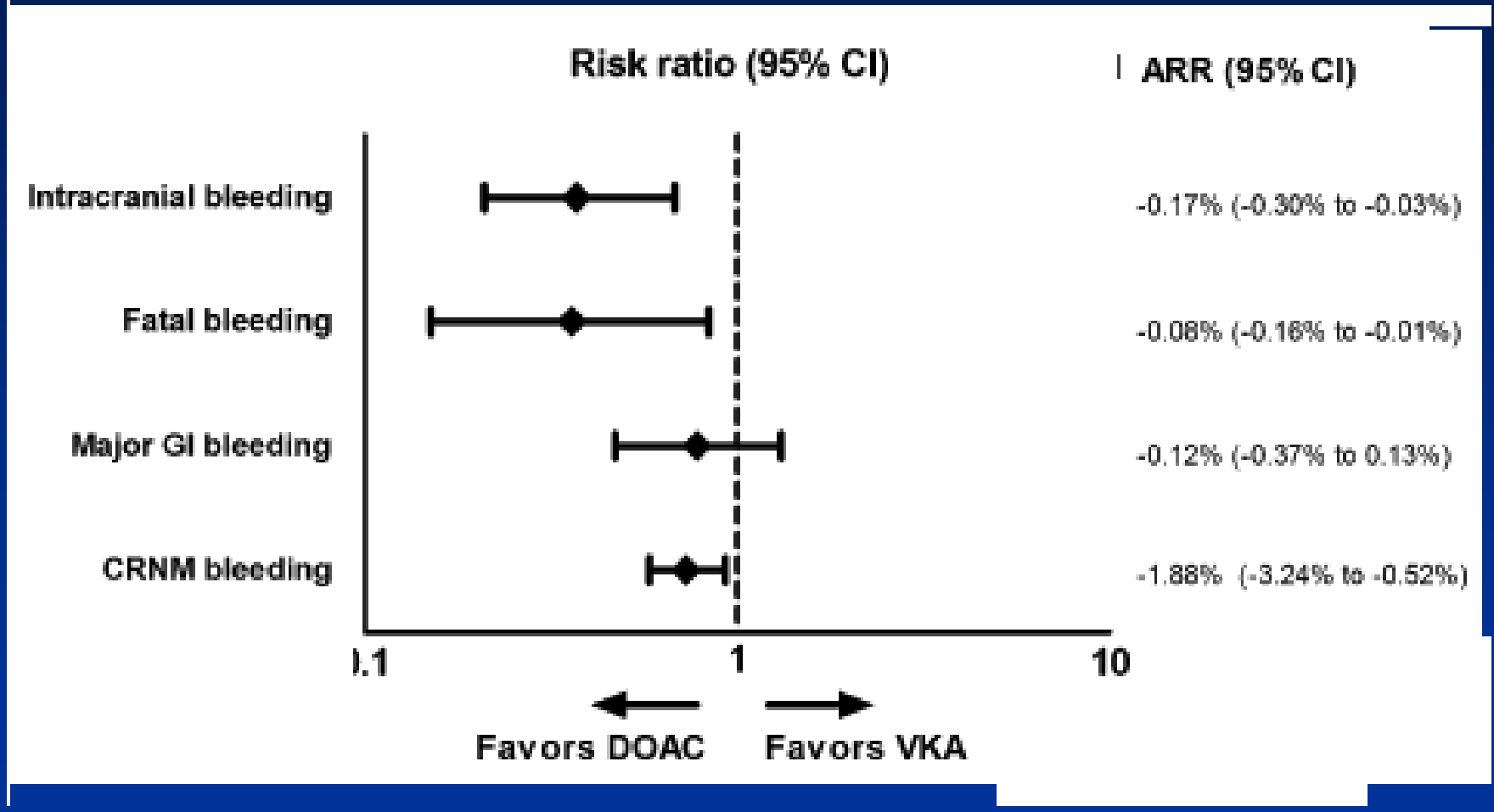
DOACs

LMWH

Direct oral anticoagulants compared with vitamin K antagonists for acute venous thromboembolism: evidence from phase 3 trials

Nick van Es,[1] Michiel Coppens,[1] Sam Schulman,[2] Saskia Middeldorp,[1] and Harry R. Büller[1]

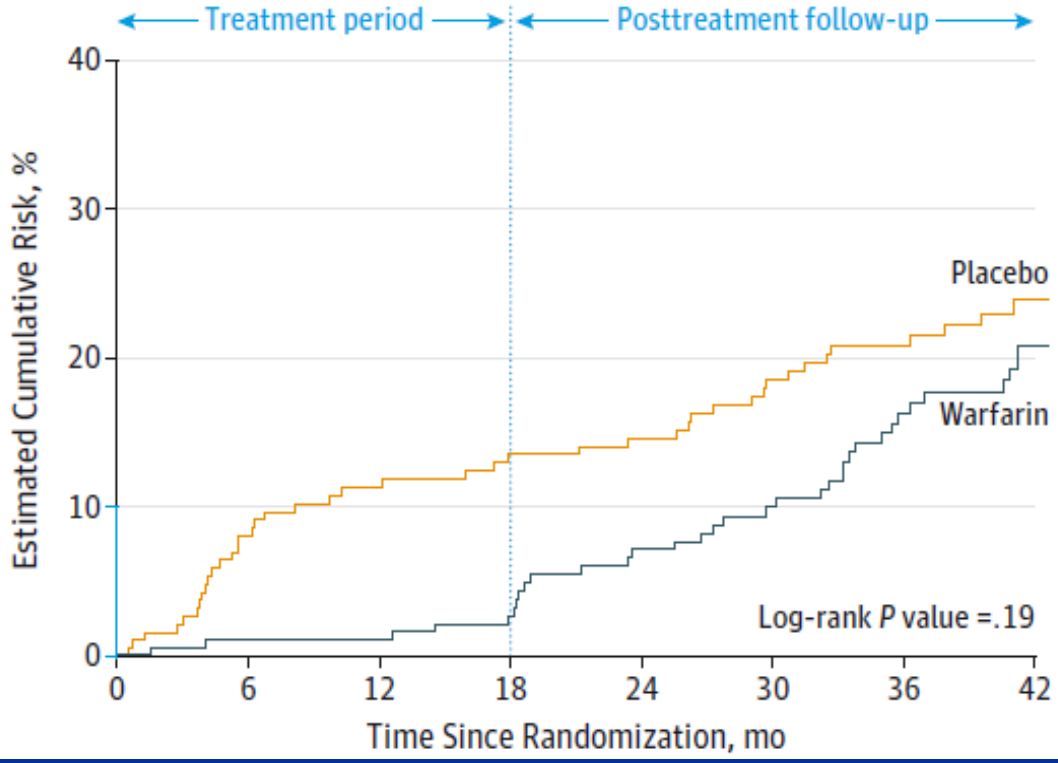
Blood 2014



Six Months vs Extended Oral Anticoagulation After a First Episode of Pulmonary Embolism
The PADIS-PE Randomized Clinical Trial

Couturaud et al.
JAMA 2015

Figure 2. Probability of the Composite Outcome of Recurrent Venous Thromboembolism and Major Bleeding Throughout the Study Period



Criteri per AC corta

I pazienti con TEV dopo chirurgia maggiore devono ricevere AC per 3 mesi (per evitare recidive)

Criteri per AC cronica

- ≥ 2 episodi documentati di TEV (TVP prossimale e/o EP)
- Cancro attivo o malattie ematologiche
- Trombofilia maggiore
- Sindrome da anticorpi antifosfolipidi
- EP con shock o grave e prolungata ipotensione a rischio vitale
- Ipertensione polmonare
- Severa insufficiency cardio-respiratoria (NYHA 3 or 4)
- Altre indicazioni per AC

Prognostic significance of residual venous obstruction in patients with treated unprovoked deep vein thrombosis

A patient-level meta-analysis

Marco P. Donadini[1]; Walter Ageno[1]; Emilia Antonucci[2]; Benilde Cosmi[3]; Michael J. Kovacs[4]; Grégoire Le Gal[5]; Paul Ockelford[6]; Daniela Poli[2]; Paolo Prandoni[7]; Marc Rodger[8*]; Giorgia Saccullo[9]; Sergio Siragusa[9]; Laura Young[10]; Matteo Bonzini[11]; Monica Caprioli[1]; Francesco Dentali[1]; Alfonso Iorio[12]; James D. Douketis[13]

At 6 mo. RVO was found in 55.1% of patients

RVO was a stronger predictor of recurrent VTE if detected at 3 months after diagnosis (HR = 2.17; 95% CI: 1.11-4.25)

Not predictive of recurrent VTE if detected at >6 months after diagnosis (1,124 patients, HR = 1.19)

CLINICAL TRIALS AND OBSERVATIONS

D-dimer to guide the duration of anticoagulation in patients with venous thromboembolism: a management study

Gualtiero Palareti,[1] Benilde Cosmi,[1] Cristina Legnani,[1] Emilia Antonucci,[2] Valeria De Micheli,[3] Angelo Ghirarduzzi,[4] Daniela Poli,[2] Sophie Testa,[5] Alberto Tosetto,[6] Vittorio Pengo,[7] and Paolo Prandoni,[8] on behalf of the DULCIS (D-dimer and ULtrasonography in Combination Italian Study) Investigators

Dopo 1 anno di terapia nessuna differenza tra chi aveva RVO (5.3%) e chi no (6.3%)

What after the first three months AC?

Accepted Manuscript

Antithrombotic Therapy for VTE Disease: CHEST Guideline

Clive Kearon, MD, PhD, Elie A. Akl, MD, MPH, PhD, Joseph Ornelas, PhD, Allen Blaivas, DO, FCCP, David Jimenez, MD, PhD, FCCP, Henri Bounameaux, MD, Menno Huisman, MD, PhD, Christopher S. King, MD, FCCP, Timothy Morris, MD, FCCP, Namita Sood, MD, FCCP, Scott M. Stevens, MD, Janine R.E. Vintch, MD, FCCP, Philip Wells, MD, Scott C. Woller, MD, Col. Lisa Moores, MD, FCCP

2016

"In patients with a first unprovoked proximal DVT of the leg or PE who have a low or moderate bleeding risk, we suggest extended anticoagulant therapy (no scheduled stop date) (Grade 2B)"

Recurrent VTE or VTE-related death in recent extension studies in placebo-treated

Trials	**Placebo group**
Resonate (6 mo; 18 mo) (dabig.)	5.6%; ~10%
Inspire (4 y) (ASA)	18.4%
Amplify extension (1 y) (apix.)	8.8%
SURVET (2 y) (sulodex.)	9.7%

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2016

Remarks:

Patient sex and D-dimer level measured a month after stopping AC therapy may influence the decision to stop or extend anticoagulant therapy.

CLINICAL TRIALS AND OBSERVATIONS

Blood 2014

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Clinical events occurred in the investigated patients

	Negative D-dimer, no anticoagulation (n = 528; 829 y)*	Positive D-dimer, anticoagulation refused (n = 109; 171 y)*	Positive D-dimer, anticoagulation resumed (n = 373; 601 y)*
Primary outcomes, n, % (95% CI)	25 (4.7%; 3.2-6.9)	15 (13.8%; 7.9-21.7)§	4 (1.1%; 0.3-2.7)
Incidence per 100 pt-y, % (95% CI)	3.0% (2.0-4.4)	8.8% (5.0-14.1)¶	0.7% (0.2-1.7)
Major bleeding, n, % (95% CI)	0	0	14‡ (3.7%; 2.1-6.2)
Incidence per 100 pt-y, % (95% CI)			2.3% (1.3-3.9)

Accepted Manuscript

Antithrombotic Therapy for VTE Disease: CHEST Guideline

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2016

In patients with a first unprovoked proximal DVT or PE and who have a:

(i) low or moderate bleeding risk, we suggest extended AC therapy (no scheduled stop date) (Grade 2B)

(ii) high bleeding risk, we recommend 3 months of AC therapy over extended therapy (Grade 1B)

All patients who receive extended AC therapy should be reassessed at periodic intervals (e.g. annually).

TABLE 11] Risk Factors for Bleeding with Anticoagulant Therapy and Estimated Risk of Major Bleeding in Low-, Moderate-, and High-Risk categories[a]

Risk Factors[b]
Age >65 y[184-193]
Age >75 y[184-188,190,192,194-202]
Previous bleeding[185,191-193,198,201-204]
Cancer[187,191,195,198,205]
Metastatic cancer[181,204]
Renal failure[185,191-193,196,199,201,206]
Liver failure[186,189,195,196]
Thrombocytopenia[195,204]
Previous stroke[185,192,195,207]
Diabetes[185,186,196,200,202]
Anaemia[185,189,195,198,202]
Antiplatelet therapy[186,195,196,202,208]
Poor anticoagulant control[189,196,203]
Comorbidity and reduced functional capacity[191,196,204]
Recent surgery[189,209,c]
Frequent falls[195]
Alcohol abuse[191,192,195,202]
Nonsteroidal anti-inflammatory drug[210]

Kearon et al.
ACCP
Chest 2016

Low risk (no bleeding factors) = 0.8%/y major bleeding
Moderate (one bleeding factor) = 1.6%/y " "
High (two or more factors) = ≥6.5%/y " "

Individual risk

Low

No AC

Moderate (?)
Personal pref.

DOACs (?)
Sulodex. (?)
ASA (?)

High

DOACs;
preferibly at low
bleeding risk

Contraind. to AC=
Sulodex., ASA

Lo studio APIDULCIS

Studio promosso dalla Fondazione;
Sperimentazione clinica con farmaco – non profit
INFORMAZIONI=
fondazionearianna@anticoagulazione.it

APIDULCIS: decisioni terapeutiche

- Al primo D-dimero positivo:
  - raccomandata AC con apixaban 2,5 mg x 2 al dì per 18 mesi
  (farmaco fornito da BMS-Pfizer)
  - esclusi se vogliono usare un altro farmaco

- Pazienti con D-dimero sempre negativo (4 volte): suggerita sospensione definitiva AC

Grazie