XXIX Congresso Nazionale FCSA
Bologna 22-23 ottobre 2018

STUDIO GIASONE

- Prof. Gualtiero Palareti
- Malattie Cardiovascolari, Università di Bologna
- Fondazione «Arianna Anticoagulazione», Bologna

fondazione arianna ANTICOAGULAZIONE

Accepted Manuscript

2016

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

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 factors) = 0.8%/y MB
Moderate (one factor) = 1.6%/y
High (two or more factors) = ≥6.5%/y “
“

Apixaban for Extended Treatment of Venous Thromboembolism

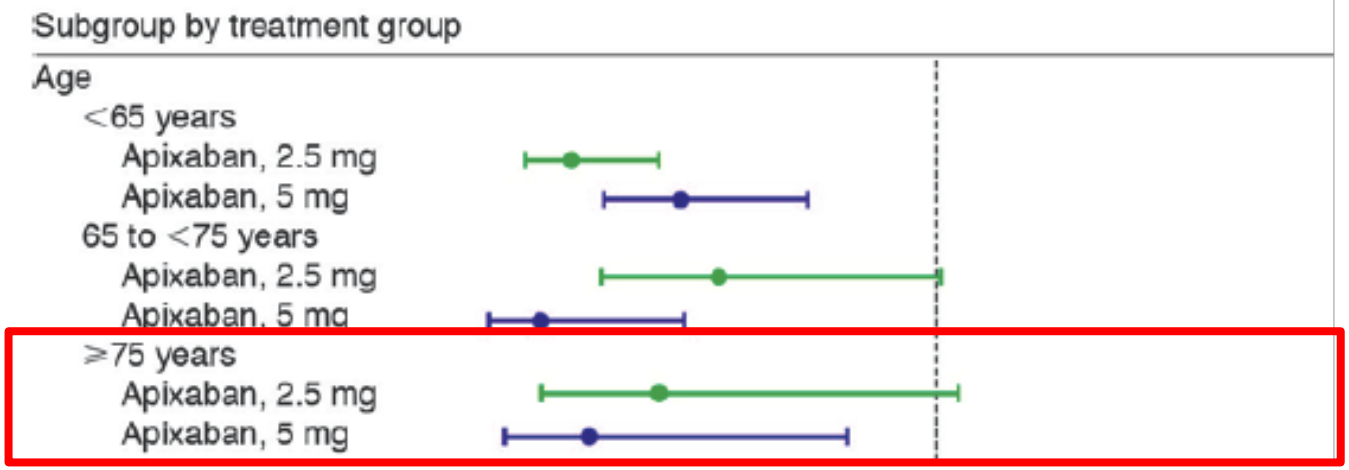
NEJM 2013

Giancarlo Agnelli, M.D., Harry R. Buller, M.D., Ph.D., Alexander Cohen, M.D., Madelyn Curto, D.V.M., Alexander S. Gallus, M.D., Margot Johnson, M.D., Anthony Porcari, Ph.D., Pharm.D., Gary E. Raskob, Ph.D., and Jeffrey I. Weitz, M.D., for the AMPLIFY-EXT Investigators*

Mean age = 56.6 y
=> 75 y = 329/2482 (13.2%)

EFFICACY

Figure S1. Relative Efficacy in the Pre-specified Subgroups of Symptomatic Recurrent Venous Thromboembolism



Apixaban for Extended Treatment of Venous Thromboembolism

NEJM 2013

Giancarlo Agnelli, M.D., Harry R. Buller, M.D., Ph.D., Alexander Cohen, M.D., Madelyn Curto, D.V.M., Alexander S. Gallus, M.D., Margot Johnson, M.D., Anthony Porcari, Ph.D., Pharm.D., Gary E. Raskob, Ph.D., and Jeffrey I. Weitz, M.D., for the AMPLIFY-EXT Investigators*

Mean age = 56.6 y

=> 75 y = 329/2482 (13.2%)

SAFETY (MB+CRNMB)

Subgroup by treatment group	Apixaban Events	Apixaban Patients	Placebo Events	Placebo Patients
Age				
<65 years				
Apixaban, 2.5 mg	11	565	13	546
Apixaban, 5 mg	21	549		
65 to <75 years				
Apixaban, 2.5 mg	9	164	8	171
Apixaban, 5 mg	9	154		
≥75 years				
Apixaban, 2.5 mg	7	111	1	109
Apixaban, 5 mg	5	108		

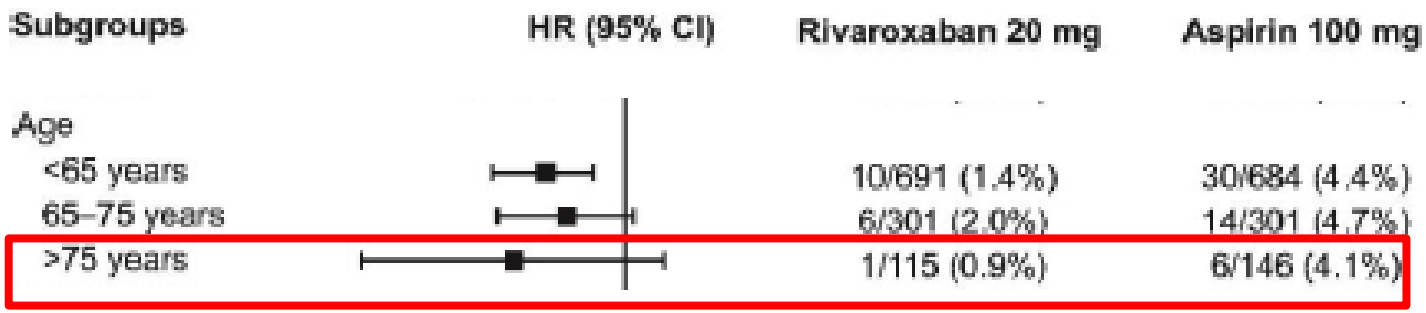
Rivaroxaban or Aspirin for Extended Treatment of Venous Thromboembolism

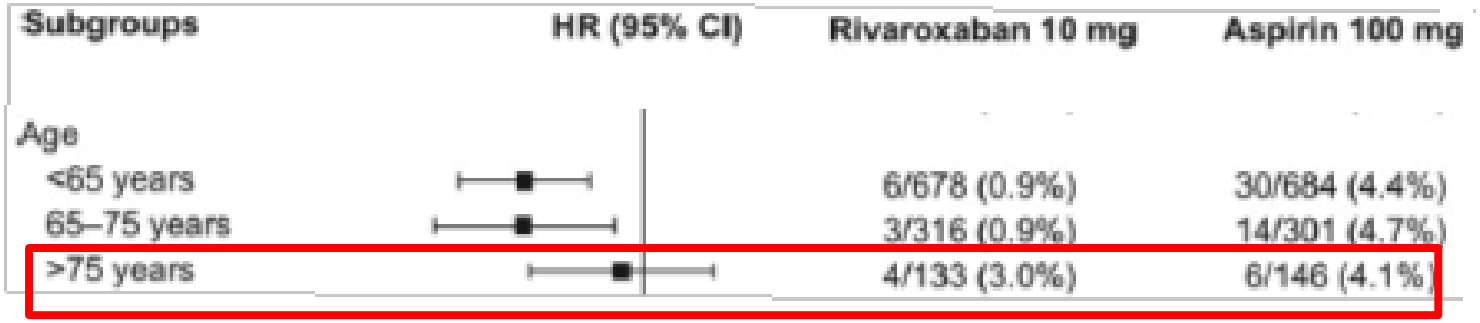
J.I. Weitz, A.W.A. Lensing, M.H. Prins, R. Bauersachs, J. Beyer-Westendorf, H. Bounameaux, T.A. Brighton, A.T. Cohen, B.L. Davidson, H. Decousus, M.C.S. Freitas, G. Holberg, A.K. Kakkar, L. Haskell, B. van Bellen, A.F. Pap, S.D. Berkowitz, P. Verhamme, P.S. Wells, and P. Prandoni, for the EINSTEIN CHOICE Investigators*

NEJM 2017

mean age = 57.9 y
=> 75 y = 394/3365 (11.7%)

EFFICACY





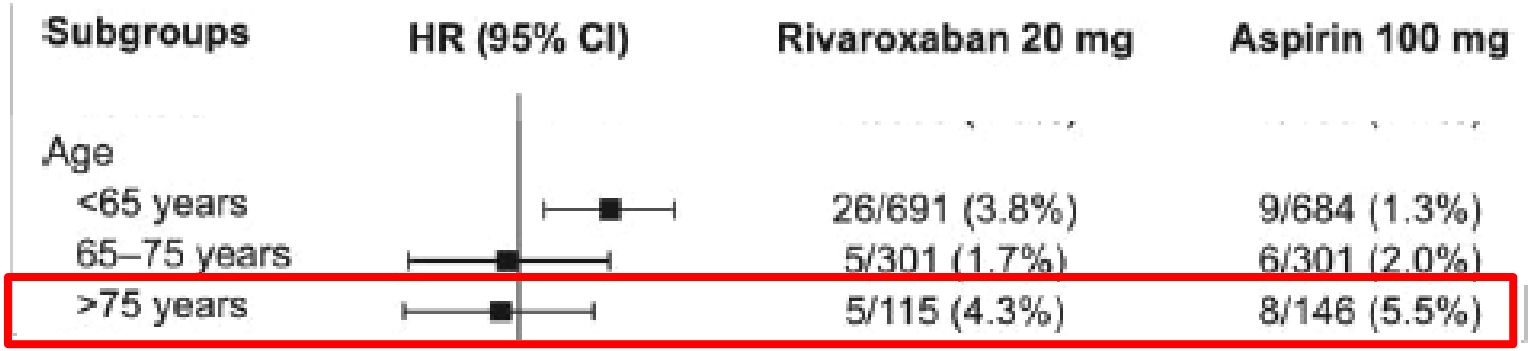
Rivaroxaban or Aspirin for Extended Treatment of Venous Thromboembolism

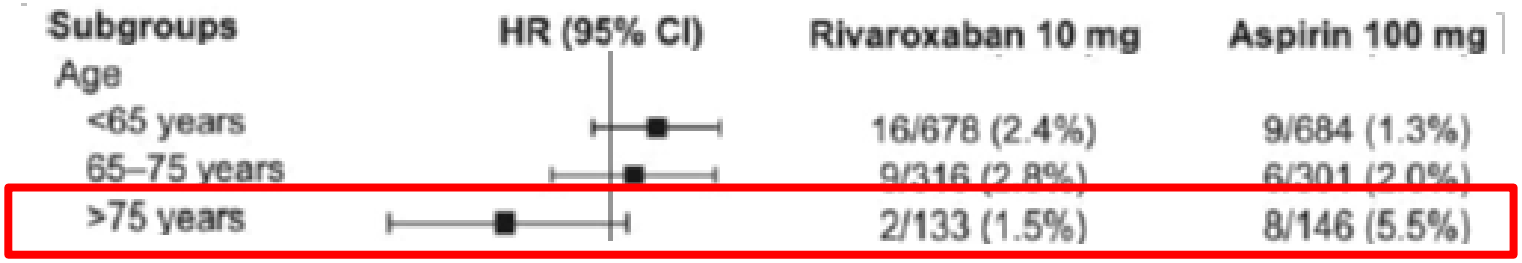
J.I. Weitz, A.W.A. Lensing, M.H. Prins, R. Bauersachs, J. Beyer-Westendorf, H. Bounameaux, T.A. Brighton, A.T. Cohen, B.L. Davidson, H. Decousus, M.C.S. Freitas, G. Holberg, A.K. Kakkar, L. Haskell, B. van Bellen, A.F. Pap, S.D. Berkowitz, P. Verhamme, P.S. Wells, and P. Prandoni, for the EINSTEIN CHOICE Investigators*

NEJM 2017

mean age = 57.9 y
=> 75 y = 394/3365 (11.7%)

SAFETY (M+CRNMB)





Comments
Extended treatment for VTE in elderly population

a) the recent extension studies with DOACs proved less satisfactory, both for efficacy and safety in elderly patients

b) Aspirin was poorly effective against recurrences, with a high rate of bleeding

Sulodexide for the Prevention of Recurrent Venous Thromboembolism

The Sulodexide in Secondary Prevention of Recurrent Deep Vein Thrombosis (SURVET) Study: A Multicenter, Randomized, Double-Blind, Placebo-Controlled Trial

Andreozzi et al. Circulation 2015

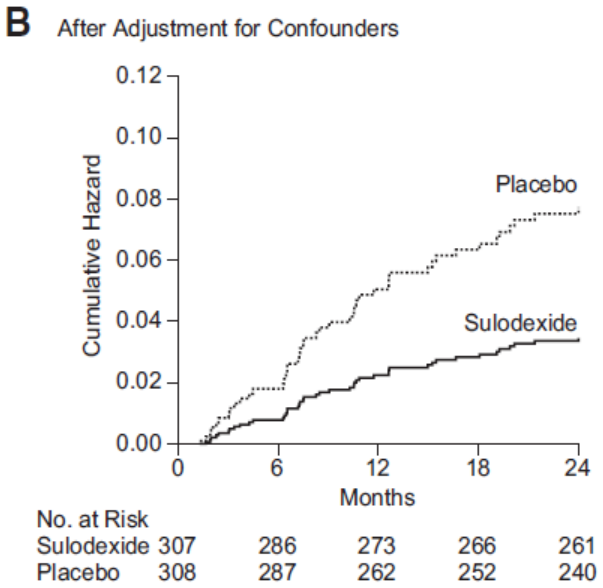


Figure 2. Risk of recurrence of venous thromboembolism in patients randomly assigned to sulodexide or placebo. **A**, Cumulative risk of recurrent venous thromboembolism. **B**, Results of an analysis of risk after adjustment for age, sex, index event (pulmonary embolism, or deep vein thrombosis), duration of anticoagulant therapy, and time from completion of anticoagulation therapy to randomization.

Sulodexide for the Prevention of Recurrent Venous Thromboembolism

The Sulodexide in Secondary Prevention of Recurrent Deep Vein Thrombosis (SURVET) Study: A Multicenter, Randomized, Double-Blind, Placebo-Controlled Trial

Andreozzi et al.
Circulation 2015

Table 2. Number of Outcome Events According to Study Group

Event	Sulodexide (n=307)	Placebo (n=308)	Hazard Ratio (95% CI)	*P* Value
Recurrent VTE				
Total episodes	15	30	0.49 (0.27–0.92)	0.025
Pulmonary embolism	3	6	0.49 (0.12–1.97)	0.32
Deep vein thrombosis	12	24	0.49 (0.25–0.99)	0.045
Bleeding				
Clinically relevant nonmajor bleeding	2	2	0.97 (0.14–6.88)	0.98

frontiers in Pharmacology

2018

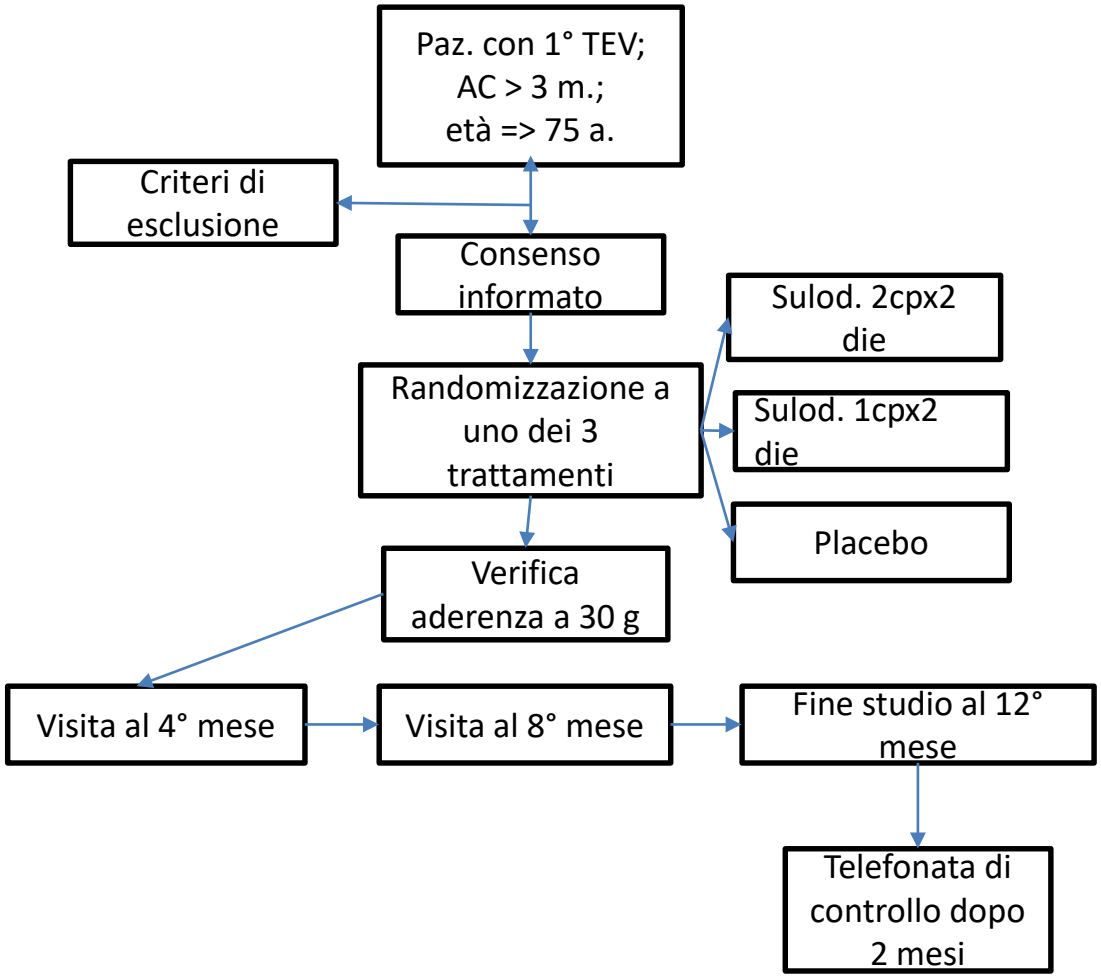
Sulodexide for Secondary Prevention of Recurrent Venous Thromboembolism: A Systematic Review and Meta-Analysis

Qing-Jun Jiang[†], Jun Bai[†], Jie Jin[†], Jian Shi[b] and Lefeng Qu[†]

Conclusions: Sulodexide could significantly reduce the recurrence of VTE after discontinuation of anticoagulation treatment as compared with placebo.

Titolo dello studio	**Studio Giasone (The Jason study)** **Prevenzione secondaria con sulodexide nei pazienti anziani dopo una trombosi venosa profonda, con o senza embolia polmonare**
Disegno	Multicentrico, italiano, randomizzato e controllato con placebo
Promotore	Fondazione Arianna Anticoagulazione (Gruppo TRIP)
Supporto	Alfasigma (farmaco+placebo+supporto economico)
Centro Coordinatore	C. Lodigiani (Humanitas, Milano)
Pazienti	$\geq$ 75 a., con 1° TVP $\pm$ EP, dopo AC per > 3 mesi,

FLOW-CHART STUDIO GIASONE



Esclusi

- < 75 anni
- Evento “provocato” (3 m. chirurgia o trauma maggiore, o allettamento > 4 giorni, o 3 m. gessi/immobilizzazione
- EP isolata (senza TVP), EP severa (rischio vitale o trombolisi)
- TVP distale isolata o in sedi diverse da arti inferiori
- Necessità di terapia anticoagulante per altri motivi
- Cancro, APLS, grave malattia associata, filtro cavale
- Antiaggreganti diversi da ASA (fino a 140 mg/die)
- Alterazioni trombofiliche maggiori
- Insufficienza cardio-respiratoria (NYHA 3 or 4)
- Impossibilità o volontà di consenso
- Aspettativa di vita < 1 anno

Trattamenti

- 3 bracci:

- Sulodexide: 2 cp x 2 volte al dì x 1 anno
- Sulodexide: 1 cp + 1 pl x 2 volte al dì x 1 anno
- Placebo: 2 pl x 2 volte al dì x 1 anno

- Randomizzazione a blocchi di 6 pazienti

Endpoint

Efficacia:

- Primario: recidiva di TVP prossimale + nuovi episodi di EP + mortalità totale per TEV
- Secondario: Eventi cardiovascolari con ricovero, morte per eventi cardiovascolari

Sicurezza:

- Primario: Incidenza di EM
- Secondario: EM + ENMCR

Obiettivi

- Efficacia: sulodexide: incidenza di recidive di TEV in pazienti anziani, con recente 1° episodio di TEV, dopo > 3 mesi di AC.

  Target: recidive: - 35% del placebo

- Sicurezza del sulodexide: non-inferiorità per EM verso placebo

  Target: EM ≈ 1% (lim. sup. confidenza non > 3%)

Attribuzione centrale degli eventi

Endpoint esaminati e attribuiti centralmente da una Commissione di 3 professionisti non partecipanti all'arruolamento e ignari del tipo di trattamento

Previsti circa 50 centri partecipanti

1° paz. previsto aprile 2019

segreteria@fondazionearianna.org