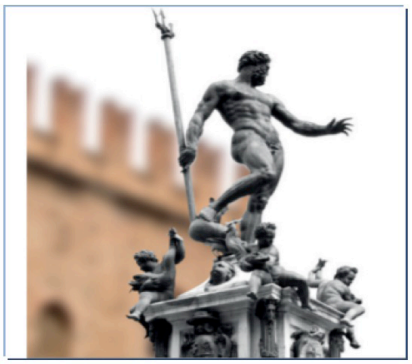


2°CONVEGNO DI ANTICOAGULAZIONE.it
scienza e pratica clinica per il management dei pazienti anticoagulati

Il ruolo attuale di eparine a basso peso molecolare e fondaparinux

Domenico Prisco
DMSC Università di Firenze
SOD Medicina Interna Interdisciplinare
AOU Careggi Firenze

Bologna 2-febbraio 2017

Disclosure

Fees for lectures and Advisory board membership:
Bayer, Boehringer Ingelheim, BMS-Pfizer, Daiichi Sankyo

Antithrombotic therapy for VTE disease: CHEST guidelines 2016

Summary of recommendations in non cancer patients

- **In patients with DVT of the leg or PE and no cancer, as long-term (first 3 months) anticoagulant therapy, we suggest dabigatran, rivaroxaban, apixaban or edoxaban over VKA therapy** (all Grade 2B).
- **For patients with DVT of the leg or PE and no cancer who are not treated with dabigatran, rivaroxaban, apixaban or edoxaban, we suggest VKA therapy over LMWH** (Grade 2C).

Kearon, Chest, 2016

Consumo di farmaci anticoagulanti per categoria terapeutica e per sostanza in Italia: anni 2007-2015

Consumo = DDD /1000 abitanti die

Sottogruppi e sostanze	2007	2008	2009	2010	2011*	2012	2013	2014	2015	Δ % 15-14
Eparine a basso peso molecolare	3,8	3,7	4,0	4,3	9,5	9,6	9,7	9,7	9,7	0,1
Antiaggreganti piastrinici escl. clopidogrel e prasugrel	56,5	59,1	60,5	61,7	64,5	65,1	63,8	59,2	59,0	-0,3
Clopidogrel da solo o in associazione	0,7	0,9	0,9	0,9	3,6	5,4	7,2	8,5	9,7	13,4
Anticoagulanti orali	5,4	5,7	5,8	6,0	6,4	6,7	6,9	6,5	6,1	-6,8
Eparina	0,2	0,2	0,2	0,1	0,5	0,5	0,5	0,6	0,4	-25,1
Nuovi antitrombotici orali	-	-	-	-	-	<0,05	0,4	2,7	6,0	123,6
Ticagrelor	-	-	-	-	-	0,1	0,3	0,5	0,6	15,6
Prasugrel	-	-	-	-	0,1	0,2	0,3	0,3	0,3	0,9
Antiaggreganti e anticoagulanti	**66,6**	**69,7**	**71,7**	**73,1**	**84,6**	**87,7**	**89,0**	**88,0**	**91,8**	**4,3**
enoxaparina	1,6	1,5	2,0	2,5	6,1	6,5	7,1	7,5	7,6	1,9
acido acetilsalicilico	38,1	40,5	42,0	43,4	57,2	58,6	58,0	54,1	54,5	0,7
nadroparina	1,3	1,5	1,3	1,1	1,4	1,5	1,6	1,4	1,4	-5,9
ticlopidina	6,5	6,8	6,8	6,6	6,7	6,2	5,5	4,7	4,0	-14,0
clopidogrel	0,7	0,9	0,9	0,9	3,5	4,7	5,9	7,1	8,1	14,2
parnaparina	0,3	0,3	0,3	0,2	0,4	0,4	0,5	0,5	0,5	0,5
fondaparinux	<0,05	0,1	0,1	0,1	0,3	0,3	0,3	0,3	0,4	34,6
warfarin	4,5	4,8	4,9	5,1	5,5	5,8	6,0	5,8	5,4	-6,2

*interruzione di serie storica

DDD: Defined Daily Dose

Fonte: AIFA - Rapporto nazionale OSMED – anno 2015

Principali indicazioni di EBPM e Fondaparinux nella pratica clinica (non tutte evidence-based)

EBPM

- Profilassi
  - Tromboembolismo venoso
- **Trattamento**
  - Trombosi Venosa Superficiale
  - Trombosi Venosa Profonda
  - Embolia Polmonare
  - Cardiopatia ischemica
  - Arteriopatia obliterante periferica
  - Alcune forme di ictus cerebrale
  - CID
  - Circolazione extracorporea

Fondaparinux

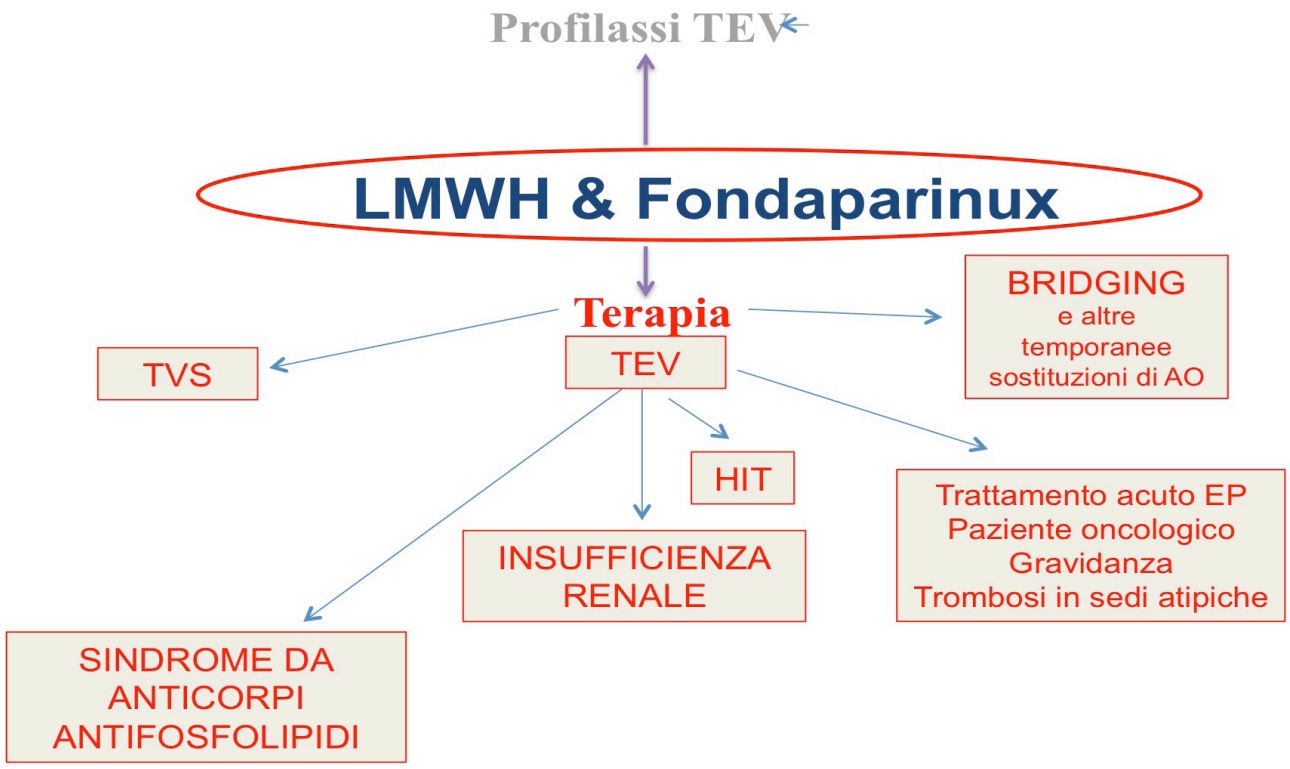
- Profilassi
  - Tromboembolismo venoso
- **Trattamento**
  - Trombosi Venosa Superficiale
  - Trombosi Venosa Profonda
  - Embolia Polmonare
  - Cardiopatia ischemica

Figura

Profilassi

Terapia
TVS
TEV in Pazienti oncologici
Trattamento TEV
Gravidanza
TEV in sedi atipiche
HIT
Insufficienza Renale
Sindrome da Anticorpi antifosfolipidi
Embricazione con farmaci orali (AVK, DAB, EDO)
Temporanea o prolungata controindicazione all'anticoagulazione
(TEV in pazienti ad alto rischio emorragico)

Pros & Cons (forse è meglio elencare le caratteristiche di entrambi i farmaci in una sorta di conclusioni per un approccio più diplomatico)



Trattamento TVS

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Fondaparinux for the Treatment of Superficial-Vein Thrombosis in the Legs

Hervé Decousus, M.D., Paolo Prandoni, M.D., Ph.D., Patrick Mismetti, M.D., Ph.D., Rupert M. Bauersachs, M.D., Zoltán Boda, M.D., Benjamin Brenner, M.D., Silvy Laporte, Ph.D., Lajos Matyas, M.D., Saskia Middeldorp, M.D., Ph.D., German Sokurenko, M.D., and Alain Leizorovicz, M.D., for the CALISTO Study Group*

Multicenter, randomized, double-blind, controlled vs placebo on efficacy and safety of Fondaparinux (Arixtra) for the treatment of SVT

Patients enrolled : 3.002
Inclusion: SVT confirmed with CUS, > 5 cm length
Exclusion: SVT < 3 cm from saphenous-femoral cross, thrombotic events < previous 6 months, active cancer, warfarin, NSAIDs, recent bleeds, platelets <100.000 plt/dl, Cr Cl< 30 ml/min

Treatments: Fondaparinux 2,5 mg or Placebo
Duration: 45 d
Follow-up: 1 month

Decousus H, NEJM 2010

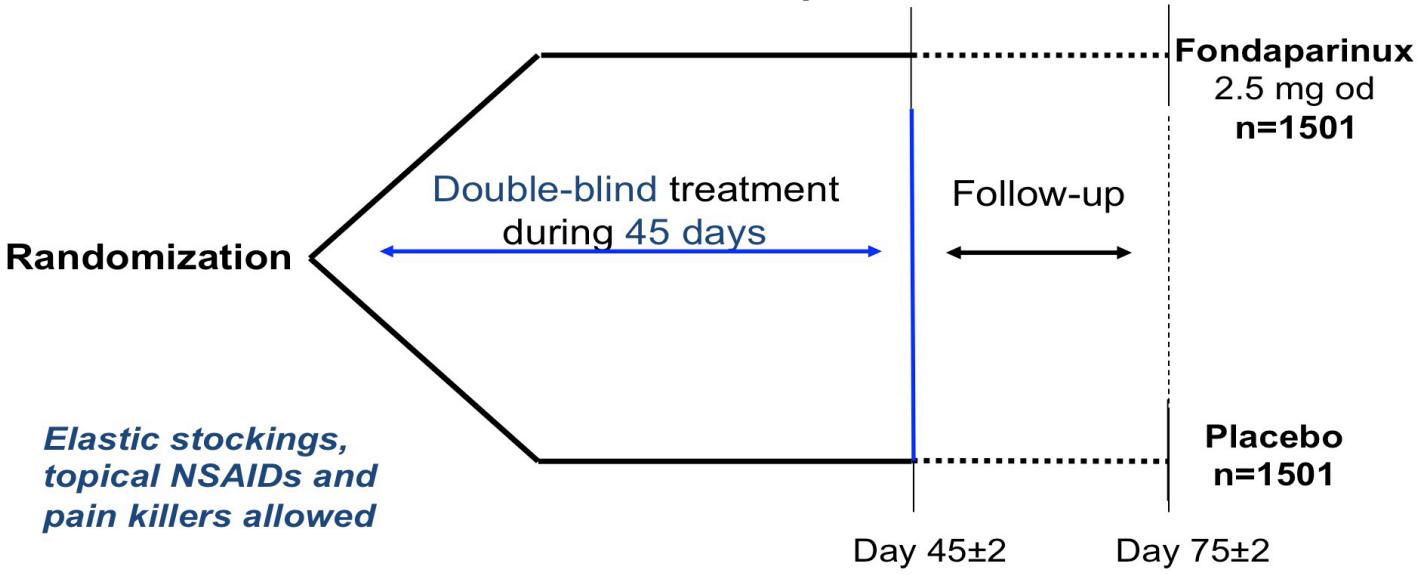
- **Primary objective:** to demonstrate the superior **efficacy** of fondaparinux 2.5 mg once daily *versus* placebo on symptomatic thromboembolic complications and/or death from any cause
- **Secondary objective:** to evaluate the **safety** of fondaparinux 2.5 mg once daily *versus* placebo on major bleeding and death

in patients with SVT of the lower limbs without concomitant DVT/PE at inclusion

Decousus H, NEJM 2010

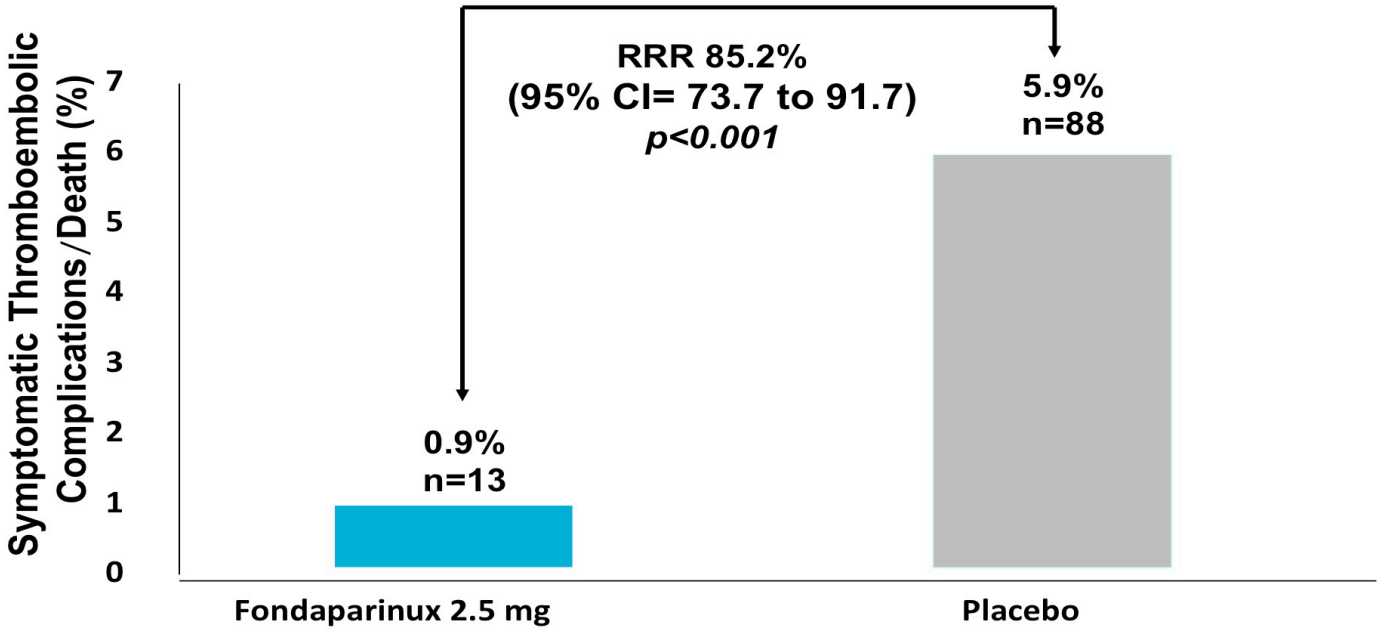
Study Design

Primary Efficacy Outcome:
Symptomatic Thromboembolic Complications/Death



Decousus H, NEJM 2010

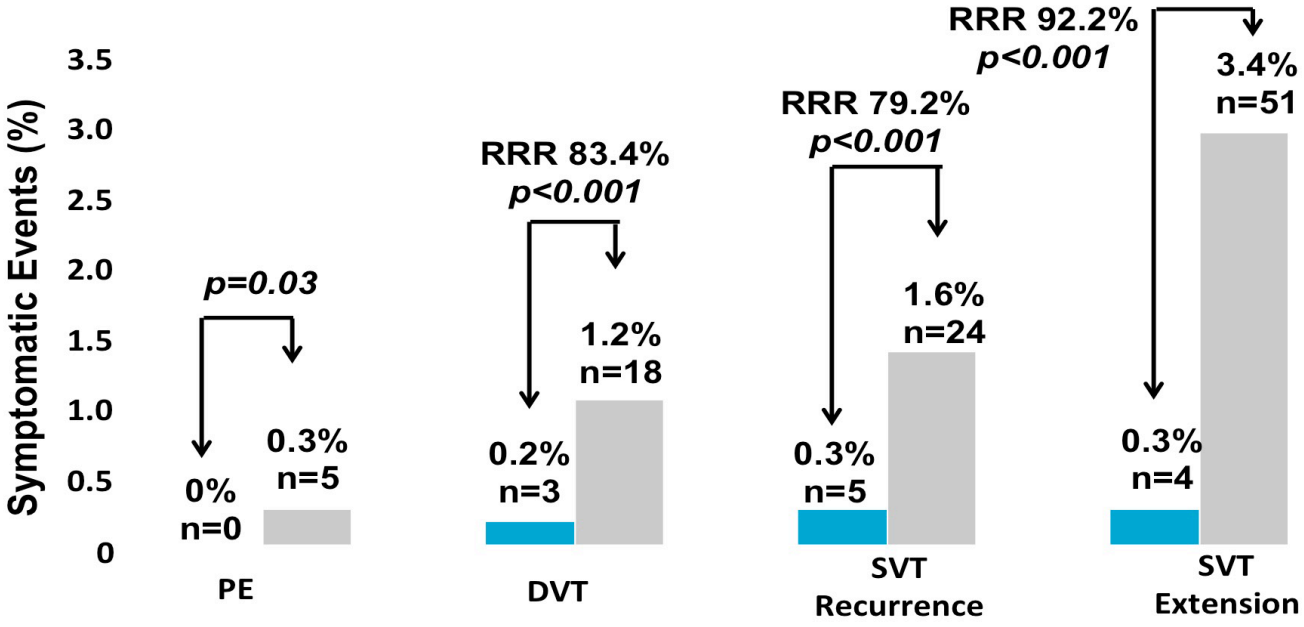
Primary Efficacy Outcome (Day 47)



Primary efficacy outcome: Symptomatic PE, DVT, Extension of the initial SVT, Recurrent SVT, All-cause death

Decousus H, NEJM 2010

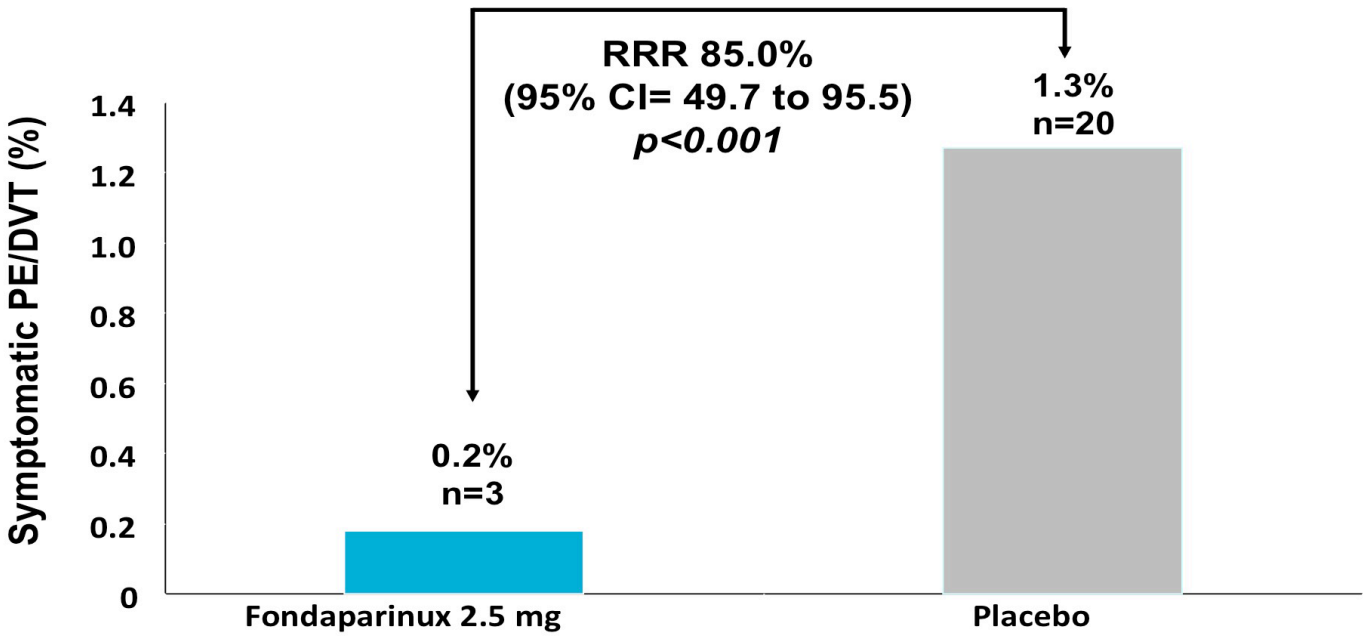
Secondary Efficacy Outcomes (Day 47)



Death: Fondaparinux=2 (cancer); Placebo =1 (heart failure)

Decousus H, NEJM 2010

Symptomatic PE or DVT (Day 47)



Symptomatic proximal DVT: Fondaparinux=1; Placebo=10
Symptomatic PE: Fondaparinux=0; Placebo=5

Decousus H, NEJM 2010

CLINICAL TRIALS AND OBSERVATIONS

Clinical relevance of symptomatic superficial-vein thrombosis extension: lessons from the CALISTO study

Alain Leizorovicz,[1] François Becker,[2] Andrea Buchmüller,[3] Isabelle Quéré,[4] Paolo Prandoni,[5] and Hervé Decousus,[3] for the CALISTO Study Group

Key Points

- Symptomatic extensions, whether or not reaching the SFJ, are common complications of SVT.
- Their frequency and associated risk of venous thromboembolic complications and medical resource consumption are reduced by fondaparinux.

Leizorovicz A Blood 2013

ORIGINAL ARTICLE

A randomized double-blind study of low-molecular-weight heparin (parnaparin) for superficial vein thrombosis: STEFLUX (Superficial ThromboEmbolism and Fluxum)

B. COSMI,* M. FILIPPINI,* D. TONTI,† G. AVRUSCIO,‡ A. GHIRARDUZZI,§ E. BUCHERINI,¶ G. CAMPORESE,** D. IMBERTI,†† and G. PALARETI,* ON BEHALF OF THE STEFLUX INVESTIGATORS[1]
*Department of Angiology & Blood Coagulation 'Marino Golinelli', S.Orsola-Malpighi University Hospital, Bologna; †Vascular Medicine Unit, Bufalini Hospital, Cesena; ‡Department of Angiology, S.Antonio Hospital, Padua; §Angiology Unit – Department of Internal Medicine, Arcispedale Santa Maria Nuova, Reggio Emilia; ¶Unit of Vascular Medicine and Angiology, Civic Hospital of Faenza, Faenza; **Unit of Angiology, University Hospital of Padua, Padua; and ††Department of Internal Medicine, G. da Saliceto Hospital, Piacenza, Italy

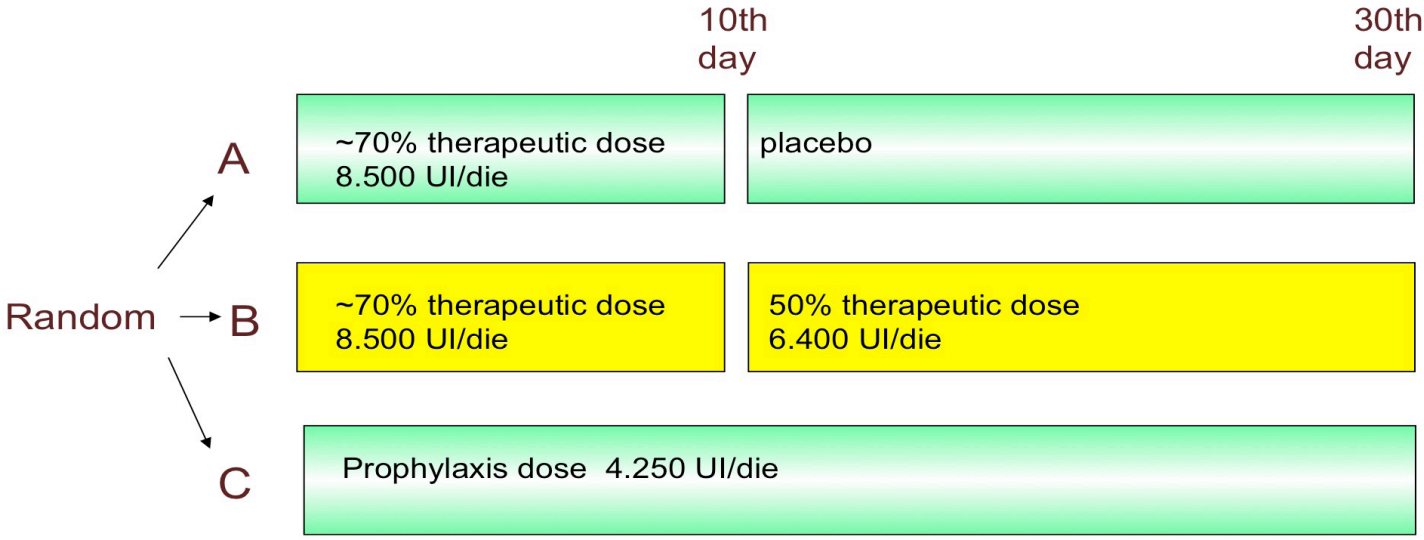
To cite this article: Cosmi B, Filippini M, Tonti D, Avruscio G, Ghirarduzzi A, Bucherini E, Camporese G, Imberti D, Palareti G, on behalf of the STEFLUX Investigators. A randomized double-blind study of low-molecular-weight heparin (parnaparin) for superficial vein thrombosis: STEFLUX (Superficial ThromboEmbolism and Fluxum). *J Thromb Haemost* 2012; **10:** 1026–35.

Multicenter, prospective, randomized, double blind (16 Centers)

Cosmi B , JTH 2012

Study Design

Phase III
Randomised, controlled, double blind, multicentre

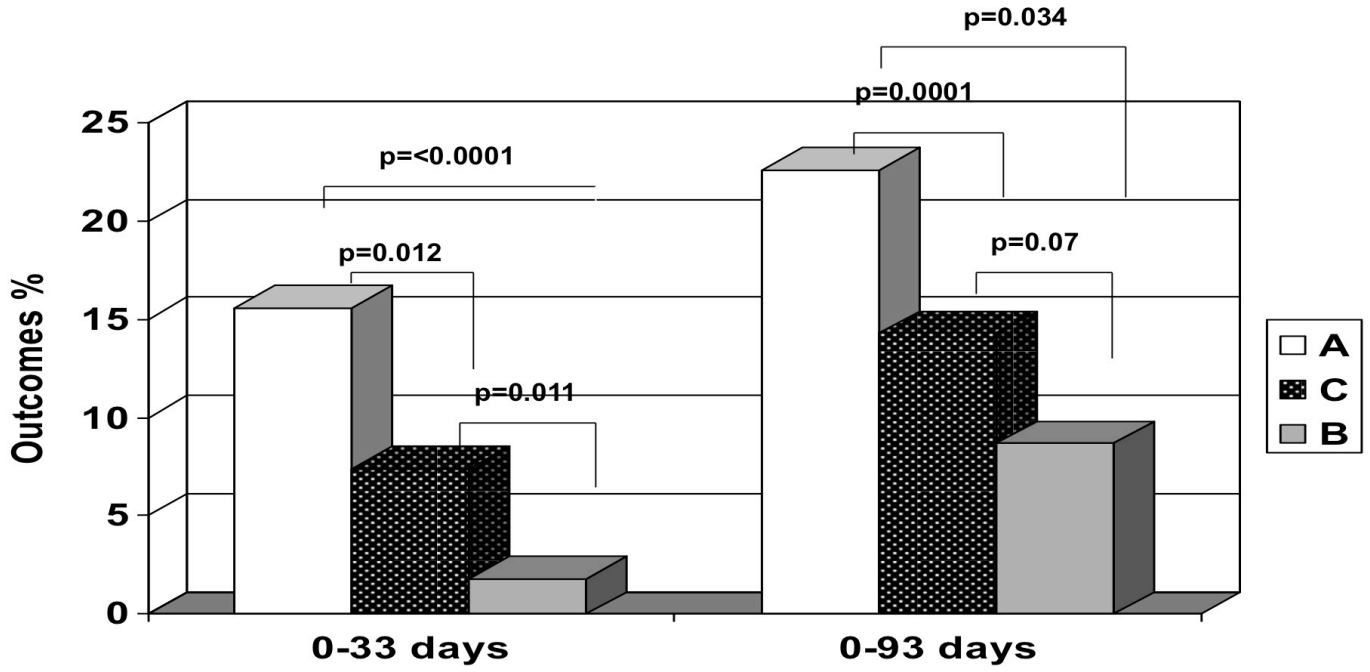


Follow-up was 60 days

Cosmi B , JTH 2012

EFFICACY OUTCOMES

(Composite of clinically relevant events and SVT extension or recurrence)



Cosmi B , JTH 2012

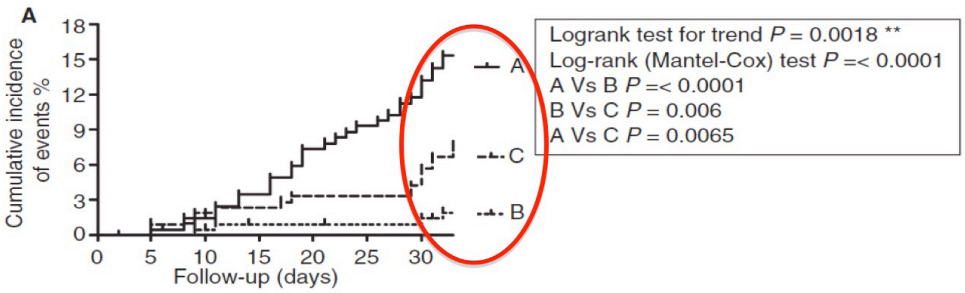
SAFETY OUTCOMES

	Group A 217	Group B 223	Group C 223	P*
0–33 days				
Total (%)	30 (13.8)	28 (12.5)	17 (7.6)	0.09
Major bleeding†	0	0	0	—
Minor bleeding	0	0	0	—
AST × 3 ULN at T0	0	0	1 (0.4)	—
AST × 3 ULN at T10	3 (1.4)	2 (0.9)	0 (0)	0.03
AST × 3 ULN at T30	0	0	1 (0.4)	0.1
ALT × 3 ULN at T0	2 (0.9)	1 (0.4)	1 (0.4)	0.76
ALT × 3 ULN at T10	16 (7.3)	17 (7.6)	6 (2.6)	0.045
ALT × 3 ULN at T30	0	1 (0.4)	3 (1.3)	0.3
Thrombocytopenia/HIT	0	0	0	—
Injection site haematomas	6 (2.7)	6 (2.6)	5 (2.2)	0.93
Allergic reactions	3 (1.4)	1 (0.4)	0	0.16
34–93 days				
Total	0	1	1	0.1
Major bleeding	0	0	0	—
Minor bleeding	0	1	1	0.1
Other	0	0	0	—

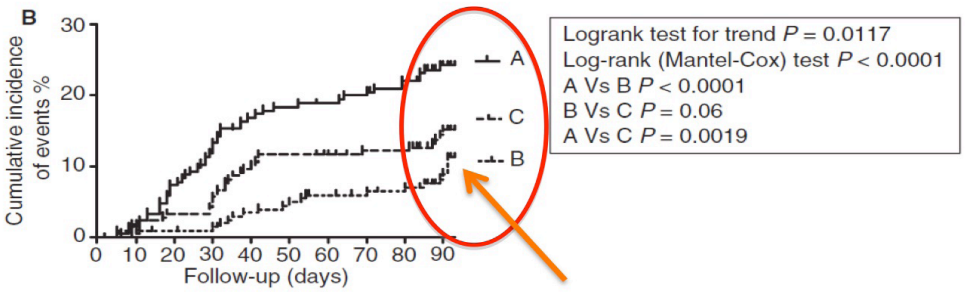
Cosmi B , JTH 2012

Cumulative incidence of events during treatment

0–33 days



0–93 days



Cosmi B, JTH 2012

Conclusion

The STEFLUX study indicates that an intermediate dose of LMWH for 30 days for acute lower limb SVT treatment is more effective in avoiding complications than prophylactic doses or a shorter period of treatment, when a composite outcome of clinically relevant events and SVT extension or recurrence are considered.

A subset of patients, however, seem to deserve a longer treatment

Cosmi B, JTH 2012

9th ACCP Consensus

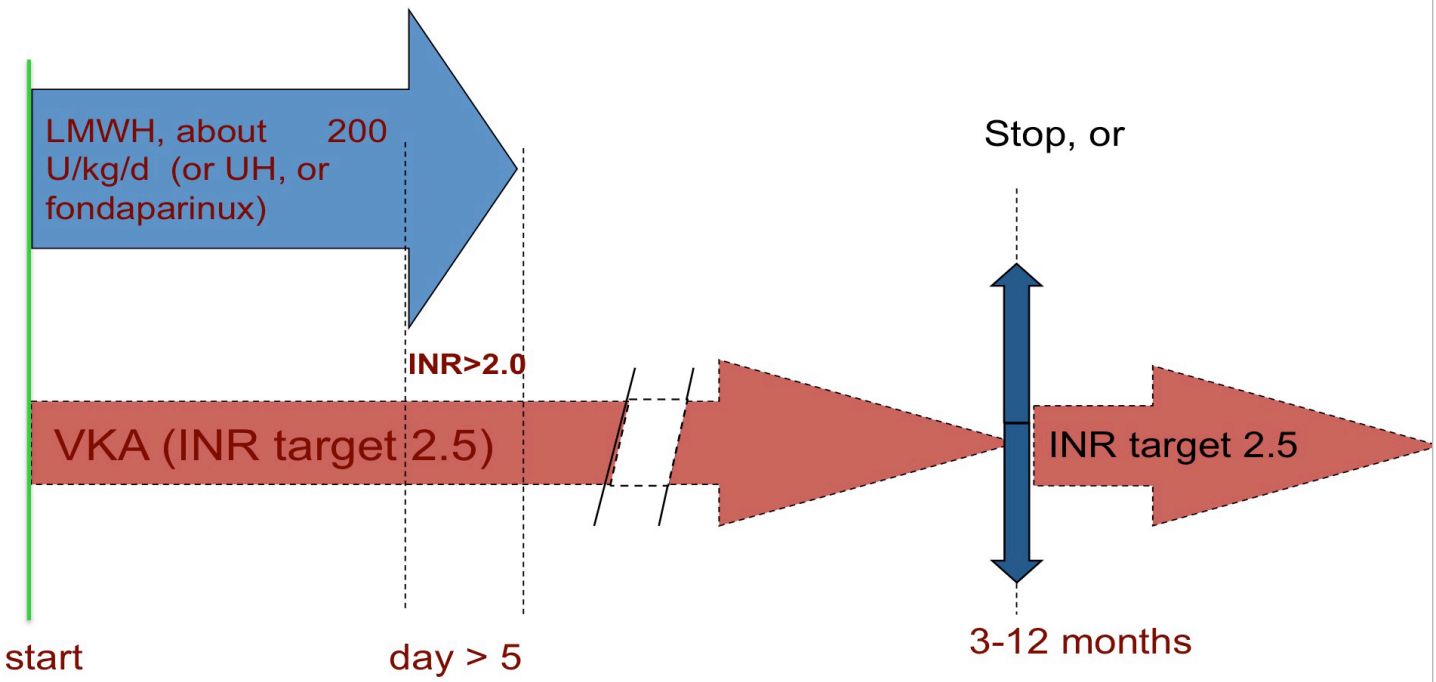
8.1.1. In patients with SVT ….of at least 5 cm in length, we suggest the use of a prophylactic dose of fondaparinux or LMWH for 45 days over no anticoagulation (Grade 2B) .

8.1.2. In patients with SVT who are treated with anticoagulation, we suggest fondaparinux 2.5 mg daily over a prophylactic dose of LMWH (Grade 2C)

Kearon et al, CHEST 2012

Trattamento TEV

VTE: standard treatment



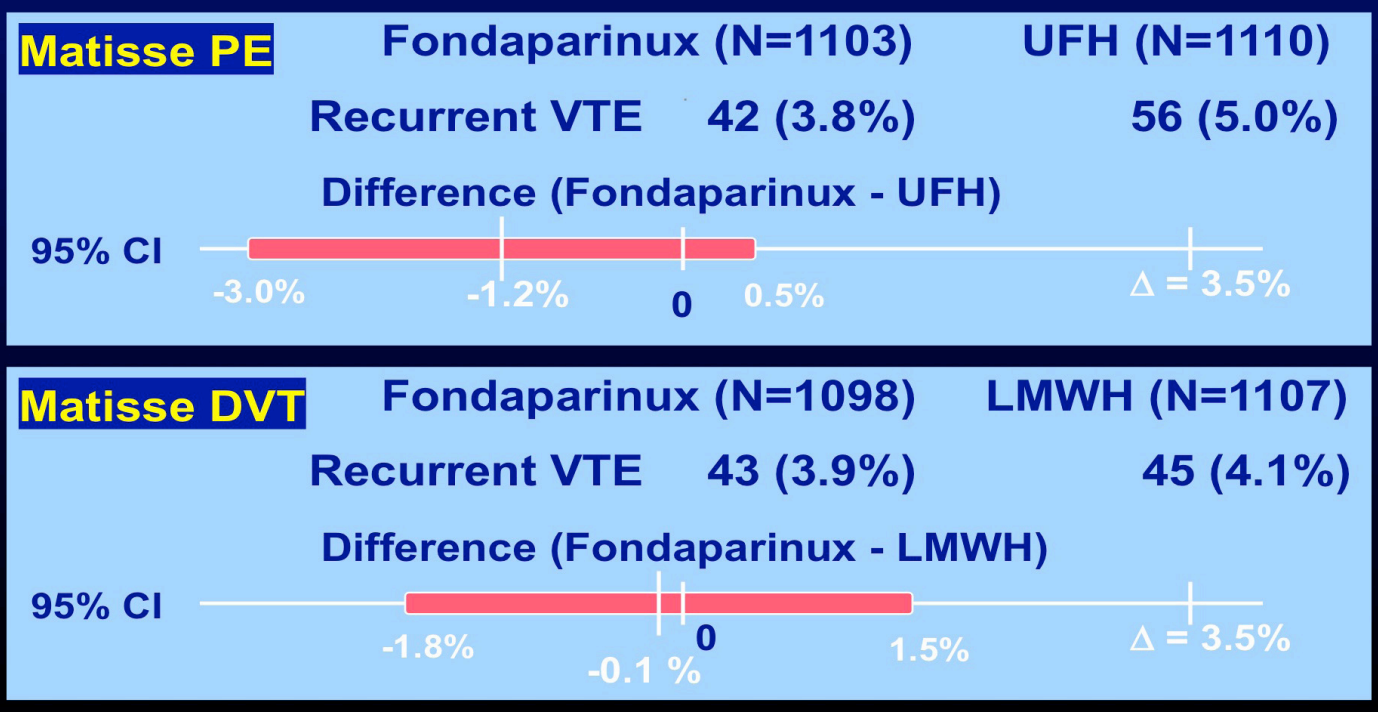
2014 ESC Guidelines on the diagnosis and management of acute pulmonary embolism

	Dosage	Interval
Enoxaparin	1.0 mg/kg or 1.5 mg/kg[a]	Every 12 hours Once daily[a]
Tinzaparin	175 U/kg	Once daily
Dalteparin	100 IU/kg[b] or 200 IU/kg[b]	Every 12 hours[b] Once daily[b]
Nadroparin[c]	86 IU/kg or 171 IU/kg	Every 12 hours Once daily
Fondaparinux	5 mg (body weight <50 kg); 7.5 mg (body weight 50–100 kg); 10 mg (body weight >100 kg)	Once daily

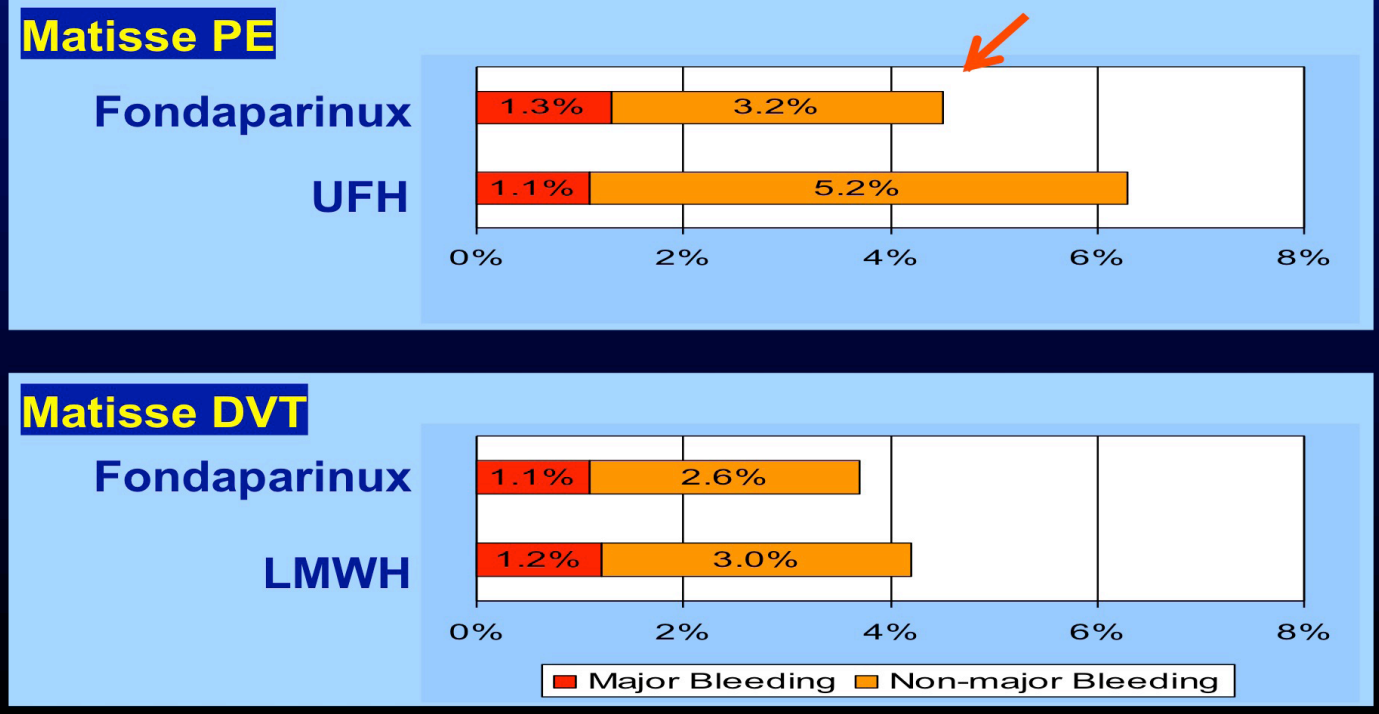
LMWH or fondaparinux are preferred over UFH for initial anticoagulation in PE, as they carry a lower risk of inducing major bleeding and heparin-induced thrombocytopenia (HIT).
UFH is recommended for patients in whom primary reperfusion is considered, as well as for those with serious renal impairment (creatinine clearance ,30 mL/min), or severe obesity.

Konstantinides S, Europ J of Cardiol 2014

Primary Efficacy Outcome



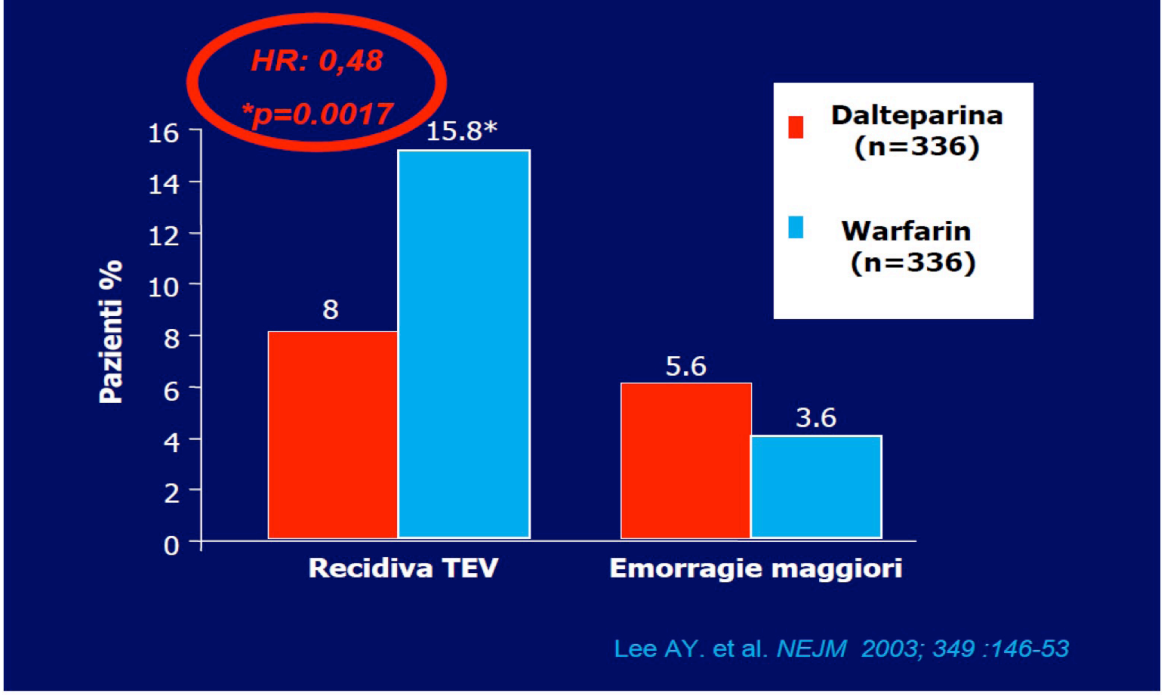
Main Safety Outcome



Trattamento paziente oncologico

STUDIO CLOT

Confronto tra Dalteparina e Warfarin per la terapia a lungo termine del TEV in pazienti neoplastici



Lee AY. et al. *NEJM 2003; 349 :146-53*

ACCP recommendations

*3. In patients with DVT of the leg or PE and cancer ("cancer-associated thrombosis"), as long-term (first 3 months) anticoagulant therapy, we suggest LMWH over VKA therapy (Grade 2C), dabigatran (Grade 2C), rivaroxaban (Grade 2C), apixaban (Grade 2C),or edoxaban (Grade 2C).

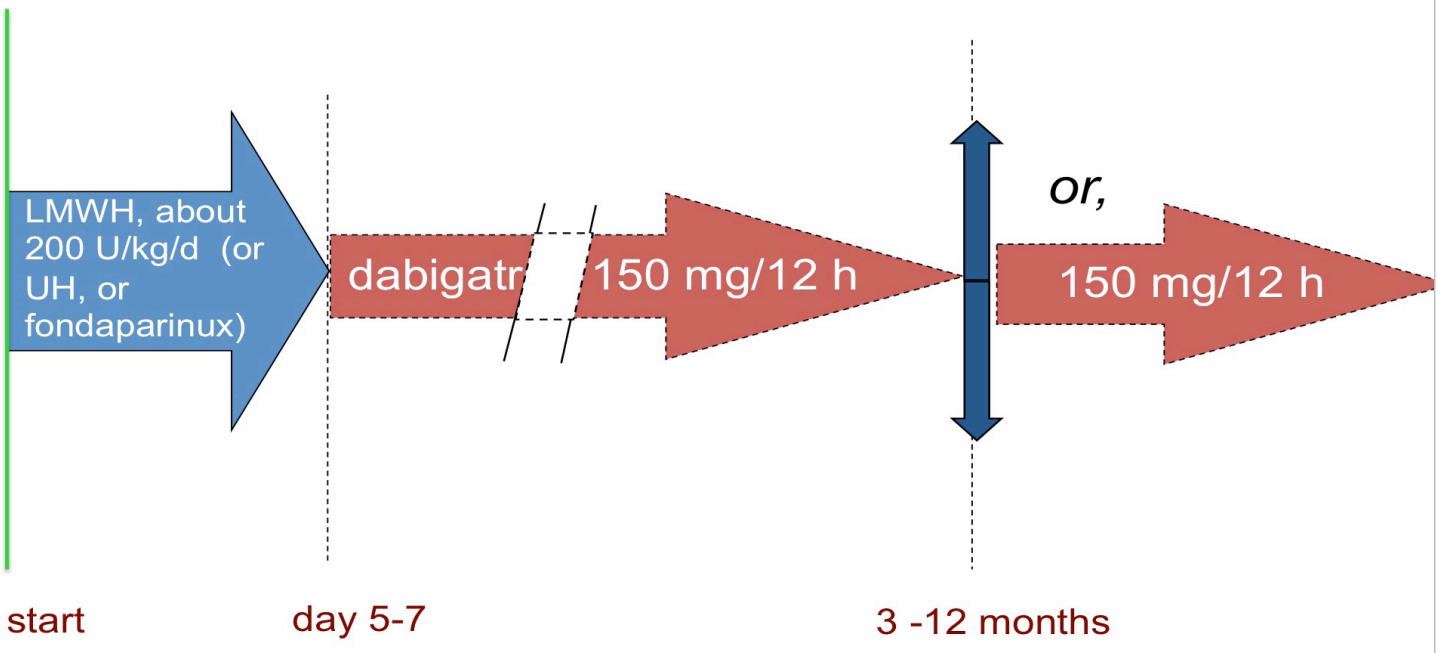
Kearon C, Chest 2016

Trattamento iniziale prima di passare a DOAC
(dabigatran e edoxaban)

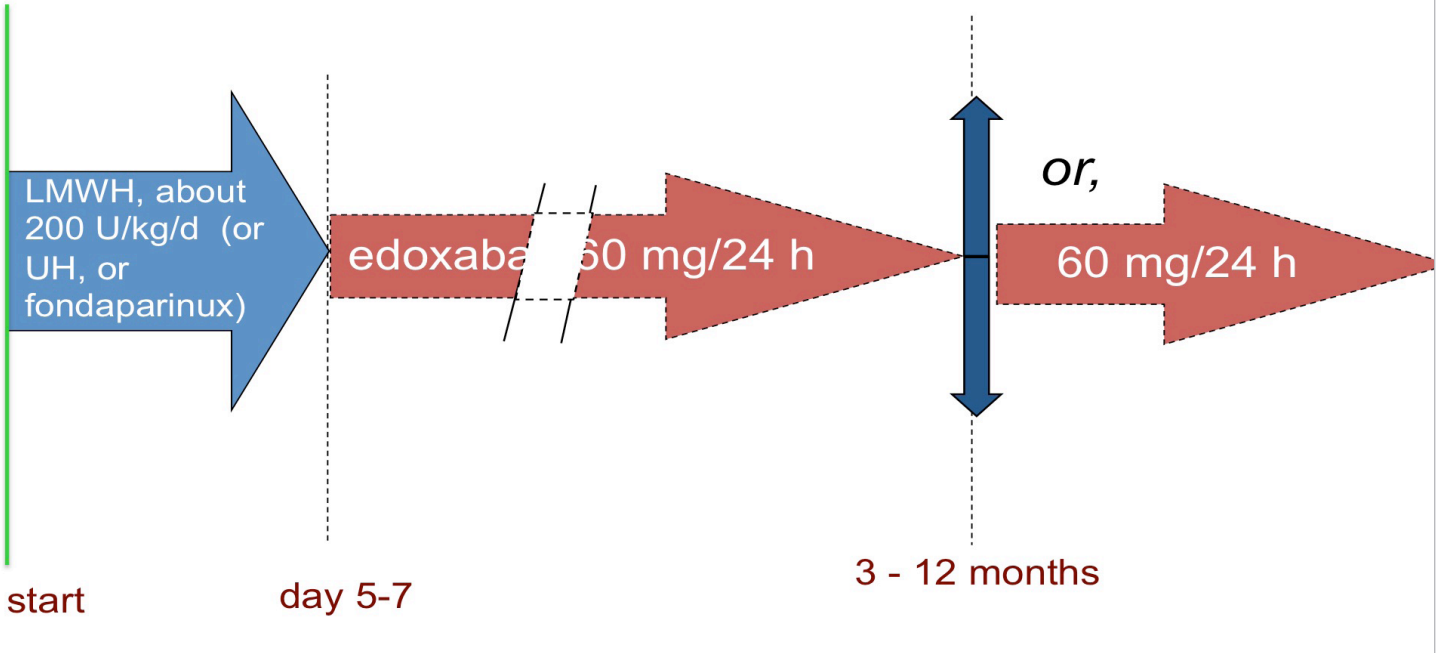
Which patients should NOT be treated with DOAC

- Patients with mechanical prosthetic heart valves and moderate/severe mitral stenosis
- Patients with contraindications to DOAC (severe renal failure -CrCl < 15 ml/min for anti-Xa-, severe liver disease with impaired haemostasis, thrombocytopenia,…)
- Patients with active bleeding or indication to surgery
- Pregnant and breast-feeding mothers

Dabigatran



Edoxaban



TEV
Situazioni Particolari

TEV
Situazioni Particolari: gravidanza

Acute VTE in pregnancy

7.1.1. For pregnant women with acute VTE, we recommend therapy with adjusted-dose subcutaneous LMWH over adjusted-dose UFH (Grade 1B)

7.1.2. For pregnant women with acute VTE, we recommend LMWH over vitamin K antagonist treatment antenatally (Grade 1A)

CHEST 2012; 141(2)(Suppl):e691S–e736S

Treatment of VTE in pregnancy
Heparin preferred over Vitamin K antagonist

LMWH is preferred because

- better bioavailability,
- longer plasma halflife,
- more predictable dose response,
- improved maternal safety profile with respect to osteoporosis and thrombocytopenia.

LMWH can be given once daily, and unlike UFH, LMWH does not require aPTT monitoring.

CHEST 2012; 141(2)(Suppl):e691S–e736S

ORIGINAL ARTICLE

Low-molecular-weight heparin for the long-term treatment of symptomatic venous thromboembolism: meta-analysis of the randomized comparisons with oral anticoagulants

A. IORIO, F. GUERCINI and M. PINI*

Results:

Seven studies that fulfillled our predefined criteria were identified, for a total of 1379 patients. When all studies were combined, **a statistically non-significant reduction in the risk of VTE (OR 0.66; 95% confidence interval [CI] 0.41, 1.07) and in the risk of major bleeding (OR 0.45; 95% CI 0.18, 1.11) in favor of LMWH treatment** was found. No difference in total mortality (OR 1.19; 95% CI 0.78, 1.83) or in cancer-related mortality was observed between the LMWH and the OA treatment.

Conclusions:

The results of this meta-analysis indicate that a 3-month course of LMWH is as effective and safe as a corresponding period of OA treatment, and **may thus be considered as a valuable alternative option for patients in whom OA treatment appears contraindicated or problematic.**

Iorio A, JTH 2003

TEV
Situazioni Particolari:
TV in sedi inusuali e APS

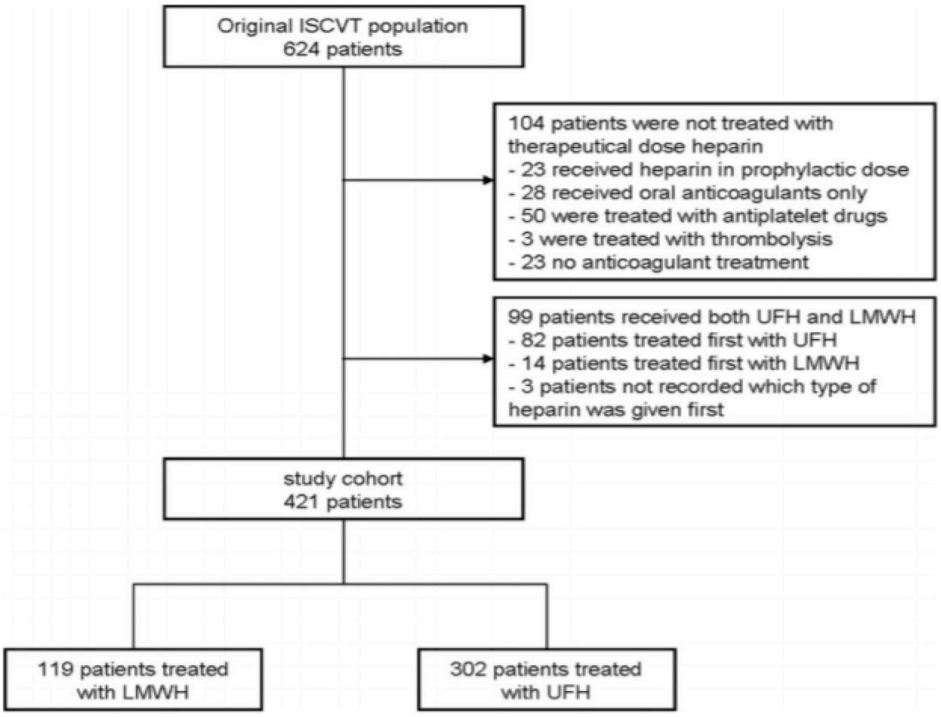
Cerebral vein thrombosis: trattamento in fase acuta

ISCVT		CEVETIS	
UFH	64%	UFH	21.9%
LMWH	34.9%	LMWH	62.7%
Antiplatelets	5.9%	Antiplatelets	0%
Thrombolysis	2.1%	Thrombolysis	1.5%

Dentali F, JTH 2012
Ferro J, Stroke 2004

Unfractionated or Low–Molecular Weight Heparin for the Treatment of Cerebral Venous Thrombosis

Jonathan M. Coutinho, MD; José M. Ferro, MD, PhD; Patrícia Canhão, MD, PhD; Fernando Barinagarrementeria, MD; Marie-Germaine Bousser, MD, PhD; Jan Stam, MD, PhD; for the ISCVT Investigators



Coutinho J, Stroke 2010

Unfractionated or Low–Molecular Weight Heparin for the Treatment of Cerebral Venous Thrombosis

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Primary and secondary end-point

	LMWH n=119	UFH n=302	Univariate Analysis		Multivariate Analysis†	
			Unadjusted OR (95% CI)	*P* Value	Adjusted OR (95% CI)	*P* Value
Primary end point						
Independency (mRS 0–2)	92%	84%	2.1 (1.0–4.2)	0.04	2.4 (1.0–5.7)	0.04
Secondary end points						
Complete recovery (mRS 0 or 1)	78%	78%	1.0 (0.61–1.7)	0.94	0.94 (0.55–1.9)	0.94
Mortality	6%	8%	0.72 (0.30–1.7)	0.47	0.81 (0.29–2.3)	0.70
New intracranial hemorrhage*	10%	16%	0.61 (0.22–1.7)	0.35	0.29 (0.07–1.3)	0.10

This nonrandomized study in patients with cerebral venous thrombosis suggests a better efficacy and safety of low–molecular weight heparin over unfractionated heparin. Low–molecular weight heparin seems preferable above unfractionated heparin for the initial treatment of cerebral venous thrombosis

Coutinho J, Stroke 2010

Cerebral vein thrombosis

Current evidence shows that patients with CVST without contraindications for AC should be treated either with body weight-adjusted subcutaneous LMWH or with dose-adjusted intravenous heparin with an at least doubled activated partial thrombo-plastin time (level B recommendation). Concomitant ICH related to CVST is not a contraindication for heparin therapy. For the reasons mentioned else-where, LMWH should be preferred in uncomplicated CVST cases

EFNS GUIDELINES

Einhaupl K, European Journal of Neurol 2010

EUROPEAN STROKE ORGANIZATION GUIDELINE ON CEREBRAL VENOUS THROMBOSIS

José M Ferro[1,2], Marie-Germaine Bousser[3], Patrícia Canhão[1,2], Jonathan M Coutinho[4], Isabelle Crassard[3], Francesco Dentali[5], Matteo di Minno[6], Alberto Maino[7], Ida Martinelli[7], Florian Masuhr[8], Diana Aguiar de Sousa[1], Jan Stam[4]

Recommendation: we recommend treating adult patients with acute cerebral venous thrombosis with heparin in therapeutic dosage. This recommendation also applies to patients with an intracerebral hemorrhage at baseline. No recommendation can be given on the treatment of children with CVT.

Quality of evidence: moderate

Strength of recommendation: strong

Recommendation: we suggest treating patients with acute cerebral venous thrombosis with low-molecular weight heparin instead of unfractionated heparin. This recommendation does not apply to patients with a contraindication for LMWH (e.g. renal insufficiency) or situations where fast reversal of the anticoagulant effect is required (e.g. patients who have to undergo neurosurgical intervention).

Quality of evidence: low

Strength of recommendation: weak

Splancnic thrombosis

- No RCTs available
- Observational studies
- Patient population heterogeneous
- GI bleeding common at presentation
- Portal hypertension common consequence

Splancnic thrombosis
ISTH Registry on SVT: Therapeutic strategies

Treatment	BCS (n: 51)	PVT (n:244)	MVT (n: 67)	SpVT (n: 19)	Multiple site (n:232)
No treatment	31.4%	33.2%	9.0%	15.8%	12.9%
UFH	15.7%	4.9%	9.0%	0	16.4%
LMWH/fonda parinux	49%	58.6%	83.6%	84.2%	71.8%
VKA	47.1%	31.6%	61.2%	63.2%	60.8%
Thrombolysis	3.9%	0	1.5%	0	2.6%

Ageno W, Seminar thromb Haemost 2014

Patients With Splanchnic Vein Thrombosis

10.1. In patients with symptomatic splanchnic vein thrombosis (portal, mesenteric, and/or splenic vein thromboses), we recommend anticoagulation over no anticoagulation (Grade 1B)

10.2. In patients with incidentally detected splanchnic vein thrombosis (portal, mesenteric, and/or splenic vein thromboses), we suggest no anticoagulation over anticoagulation
(Grade 2C)

CHEST 2012; 141(2)(Suppl):7S–47S

DOACs e APS

- Problemi metodologici per diagnosi di aPL durante terapia con DOACs
- Pazienti con APS esclusi dai trial del TEV
- Non risultati di studi controllati
- Descritti risultati di piccole serie
- Studio TRAPS in corso

Therapeutic Dose of LMWH in Patients With Decreased Renal Function

7.1. For patients receiving therapeutic LMWH who have severe renal insufficiency (calculated creatinine clearance , 30 mL/min), we suggest a reduction of the dose rather than using standard doses (Grade 2C)

CHEST 2012; 141(2)(Suppl):7S–47S

Bridging

SERIE GENERALE

Spediz. abb. post. - art. 1, comma 1
Legge 27-02-2004, n. 46 - Filiale di Roma

Anno 157° - Numero 183

GAZZETTA UFFICIALE

DELLA REPUBBLICA ITALIANA

PARTE PRIMA — Roma - Sabato, 6 agosto 2016 — SI PUBBLICA TUTTI I GIORNI NON FESTIVI

DETERMINA 20 luglio 2016.

Inserimento delle eparine a basso peso molecolare (EBPM) nell'elenco dei medicinali per uso umano erogabili a totale carico del Servizio sanitario nazionale, ai sensi della legge 23 dicembre 1996, n. 648, per il trattamento del tromboembolismo nella sospensione degli anti-vitamina K (AVK) per manovre chirurgiche e/o invasive (*bridging*). (Determina n. 999/2016).

Bridging
Criteri di inclusione ed esclusione

SERIE GENERALE
Anno 157° - Numero 183
GAZZETTA UFFICIALE
DELLA REPUBBLICA ITALIANA
PARTE PRIMA Roma - Sabato, 6 agosto 2016

Denominazione: eparine a basso peso molecolare (EBPM).

Indicazione terapeutica: trattamento del tromboembolismo nella sospensione degli anti-vitamina K (AVK) per manovre chirurgiche e/o invasive (*bridging*).

Criteri di inclusione: pazienti a rischio basso, moderato ed elevato di tromboembolismo.

Criteri di esclusione: pazienti sottoposti a procedure con minimo rischio di sanguinamento (procedure dermatologiche minori come escissione di tumori basali e squamosi, cheratosi attiniche e nevi, cataratta con anestesia topica (non retrobulbare), avulsioni dentarie semplici, igiene dentaria (detartrasi), biopsie ossee).

Periodo di prescrizione a totale carico del Servizio sanitario nazionale: fino a nuova determinazione dell'Agenzia italiana del farmaco.

Dosaggio giornaliero per via sottocutanea di EBPM per pazienti con rischio basso e moderato di tromboembolismo

EBPM	Dosaggio giornaliero
Nadroparina	2850-3800-5700 U/die
Enoxaparina	4000 U/die
Reviparina	1750-4200 U/die
Dalteparina	5000 U/die
Bemiparina	3500 U/die
Parnaparina	4250 U/die

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PARTE PRIMA Roma - Sabato, 6 agosto 2016

Dosaggio giornaliero per via sottocutanea per il bridging da terapia anticoagulante orale (TAO) a EBPM a dosi intorno al 70% di quelle terapeutiche

Dosaggio giornaliero per peso corporeo	Nadroparina	Enoxaparina	Dalteparina	Reviparina	Parnaparina	Bemiparina
< 50 kg	2850 U × 2 = 0.3 cc × 2/die	2000 U × 2 = 0.2 cc × 2/die	-------	-------	3200 U × 2/die	3500 U × 1/die
50-69 kg	3800 U × 2 = 0.4 cc × 2/die	4000 U × 2 = 0.4 cc × 2/die	7500 U × 1/die	4200 U × 2/die	4250 U × 2/die 5	-------
70-89 kg	5700 U × 2 = 0.6 cc × 2/die	6000 U × 2 = 0.6 cc × 2/die	10000 U × 1/die	-------	6400 U × 2/die	-------
90-110 kg	7600 U × 2 = 0.8 cc × 2/die	8000 U × 2 = 0.8 cc × 2/die	12500 U × 1/die	6300 U × 2/die	-------	7500 U × 1/die
> 110 kg	9500 U × 2 = 1.0 cc × 2/die	10000 U × 2 = 1.0 cc × 2/die	15000 U × 1/die	6300 U × 2/die	-------	-------

Piano Terapeutico

previsione fino a 10 giorni, dosaggi profilattici o terapeutici di EBPM a seconda del rischio tromboembolico.
Rischio basso moderato: dosaggio profilattico; rischio elevato: dosaggio subterapeutico (70 % della dose terapeutica)

BRIDGING: *Dati da inserire nel Registro*

	Sanguinamento a 7 giorni	Eventi tromboembolici a 30 giorni
Tipo di intervento chirurgico		
Tipo di procedura invasiva		

Istituzione del registro

Rilevamento e trasmissione dei dati di monitoraggio clinico e informazioni riguardo a sospensioni del trattamento

Acquisizione del consenso informato

Modalità di prescrizione e di dispensazione del medicinale

Rilevamento e trasmissione dei dati di spesa

FONDA o EBPM?

CLINICAL TRIALS AND OBSERVATIONS

Fondaparinux for the treatment of suspected heparin-induced thrombocytopenia: a propensity score–matched study

Matthew Kang,[1] Majed Alahmadi,[1] Sonja Sawh,[2] Michael J. Kovacs,[1] and Alejandro Lazo-Langner[1,3]

[1]Department of Medicine, Division of Hematology, University of Western Ontario, London, ON, Canada; [2]Pharmacy Services, London Health Sciences Centre, London, ON, Canada; and [3]Department of Epidemiology and Biostatistics, University of Western Ontario, London, ON, Canada

- We retrospectively evaluated 239 patients who received a nonheparin anticoagulant (fondaparinux 5133, danaparoid 559, and argatroban 547) for suspected or confirmed HIT.
- A propensity score was constructed based on age, gender, creatinine, 4T scores, and comorbidity index, and used to match 133 patients to 60 controls.
- Outcomes were thrombosis or thrombosis-related death and major bleeding.
- In the matched population there were 22 (16.5%) episodes of thromboses in the fondaparinux group and 13 (21.4%) in the control group.

Kang M, Blood 2015

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- Bleeding was observed in 28 (21.1%) patients in the fondaparinux group compared with 12 (20%) in the control group.
- Survival analysis, and subgroup and unmatched analyses showed similar results.
- In the fondaparinux group, 60% of patients received prophylactic doses.
- Fondaparinux has similar effectiveness and safety as argatroban and danaparoid in patients with suspected HIT.
- Prophylactic fondaparinux doses seem to be effective if no indication for full anticoagulation exists

Kang M, Blood 2015

Journal of Thrombosis and Haemostasis, **5**: 1191–1194

ORIGINAL ARTICLE

Effect of obesity on outcomes after fondaparinux, enoxaparin, or heparin treatment for acute venous thromboembolism in the Matisse trials

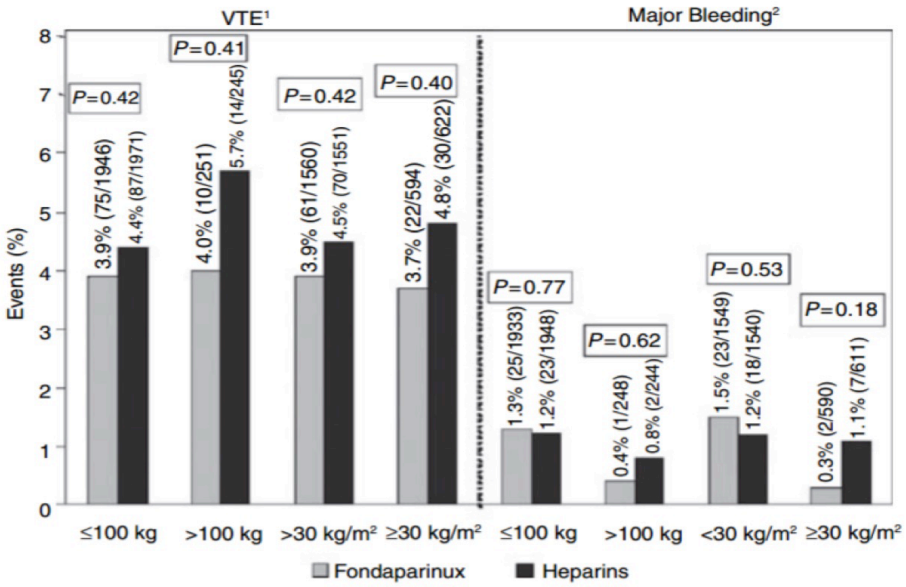
B. L. DAVIDSON,* H. R. BÜLLER,† H. DECOUSUS,‡ A. GALLUS,§ M. GENT,¶ F. PIOVELLA,** M. H. PRINS,†† G. E. RASKOB,‡‡ A. E. M. SEGERS† and A. W. A. LENSING†, FOR THE MATISSE INVESTIGATORS

Anticoagulant	Dosage (>100 Kg, 100-216 Kg)
Fondaparinux	10 mg
Enoxaparina	220 U (106-344)
Eparina NF	33.460 U (6000-82184)

To use the Matisse trials comparison of sc fondaparinux once daily with control heparin therapies (intravenous unfractionated heparin for pulmonary embolism, sc enoxaparin 1 mg/kg b.i.d. for deep vein thrombosis) for initial treatment in order to compare primary outcomes (venous thromboembolism recurrence and major bleeding) in obese patients.

Davidson J , JTH 2007

RESULTS



The incidences of recurrence and major bleeding were similar for each patient subset of weight and BMI for both fondaparinux and heparin treatment groups.

The current recommended doses of fondaparinux and heparins for the treatment of venous thromboembolism appear to provide similar protection against recurrence and major bleeding to one another and to obese and non-obese patients. ***Davidson J , JTH 2007***

Fondaparinux
Dose Management by Weight

8.1. For patients with VTE and body weight over 100 kg, we suggest that the treatment dose of fondaparinux be increased from the usual 7.5 mg to 10 mg daily SC (Grade 2C)

CHEST 2012; 141(2)(Suppl):7S–47S

Conclusioni

EBPM- Riflessioni

- ✓ Le EBPM sono caratterizzate da profili farmacodinamici e farmacocinetici più favorevoli rispetto all'eparina non frazionata (buona correlazione tra dose ed effetto anticoagulante; monitoraggio terapeutico non necessario nella maggior parte dei casi)
- ✓ Emorragia cerebrale o alto rischio di sanguinamento non sono una controindicazione al trattamento con EBPM
- ✓ Sono l'unico trattamento attualmente disponibile per alcune indicazioni (TEV in gravidanza e cancro)

Fondaparinux- Riflessioni

- è più efficace del placebo per la cura e la prevenzione delle complicanze delleTVS
- è altrettanto efficace e sicuro dell'eparina per la terapia del TEV
- **Monosomministrazione**
- Pazienti **obesi** ben rappresentati negli studi
- è più efficace del placebo per la prevenzione del TEV in pazienti ospedalizzati nei reparti di medicina
- Dose validata in profilassi per pz con **insufficienza renale moderata**
- **No HIT**
- **No allergie**

Conclusioni

- Le EBPM ed il fondaparinux rappresentano un presidio terapeutico efficace e relativamente sicuro per molte indicazioni cliniche

- Non sembrano essere presenti ad oggi farmaci che potranno sostituirli a breve, specie per alcune indicazioni