

Clinical trials of heparin (UFH or LMWH) for venous thrombosis in all type of patients

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1 anticoagulant

Trial	Treatments	Patients	Trials design and methods
warfarin vs discontinuation			
PREVENT (Ridker) , 2003 n=255/253 follow-up: 2.1 years	extension with low-intensity warfarin (target INR, 1.5 to 2.0) versus placebo	Patients with idiopathic venous thromboembolism who had received full-dose anticoagulation therapy for a median of 6.5 months	Parallel groups
Agnelli , 2003 n=NA follow-up: 33 months	continuation for 3 or 9 additional months of warfarin or other oral anticoagulant was adjusted to achieve a target INR between 2.0 and 3.0. versus discontinuation (after 3 months)	patients who had had 3 months of oral anticoagulant therapy without experiencing recurrence or bleeding after a first episode of pulmonary embolism	Parallel groups open Italy
Agnelli , 2001 n=NA follow-up: 33 months	continuation for 9 additional months; warfarin or acenocoumarol adjusted to achieve a target INR between 2.0 and 3.0 versus discontinuation (after 3 months months)	Patients with a first episode of idiopathic proximal deep venous thrombosis who had completed three months of oral anticoagulant therapy	Parallel groups open Italy
LAFIT (Kearon) , 1999 n=NA follow-up:	Continuation of the oral anticoagulant therapy up to 24 months, warfarin was adjusted to achieve a target INR between 2.0 and 3.0. versus discontinuation (after 3 months)	patients who had completed 3 months of anticoagulant therapy for a first episode of idiopathic venous thromboembolism	
ELAET (Kearon) , 2004 n=NA follow-up: 11 months (after randomizatio)	continuation for 2 additional months of warfarin adjusted to achieve a target INR between 2.0 and 3.0. versus discontinuation (after 1 months)	-	Parallel groups double blind Canada, US
Levine , 1995 n=NA follow-up: 11 months after randomization.	continuation for 2 months of warfarin adjusted INR value of 2.0 to 3.0 versus Discontinue oral anticoagulant therapy (after 1 months)	Patients with venographically confirmed acute proximal DVT who had received four weeks of warfarin after initial heparin and whose four week IPG was normal	Parallel groups double blind Canada, Italy
DURAC (Schulman) , 1997 n=NA follow-up: Four years after randomization	indefinite warfarin or dicoumarol adjusted for a target INR between 2.0 and 2.85 versus 6 months warfarin or dicoumarol adjusted for a target INR between 2.0 and 2.85	-	Parallel groups open Sweden

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Kearon C, Gent M, Hirsh J, Weitz J, Kovacs MJ, Anderson DR, Turpie AG, Green D, Ginsberg JS, Wells P, MacKinnon B, Julian JA A comparison of three months of anticoagulation with extended anticoagulation for a first episode of idiopathic venous thromboembolism. *N Engl J Med* 1999;340:901-7 [10089183]

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2 extended anticoagulant

Trial	Treatments	Patients	Trials design and methods
warfarin vs discontinuation			
PREVENT (Ridker) , 2003 n=255/253 follow-up: 2.1 years	extension with low-intensity warfarin (target INR, 1.5 to 2.0) versus placebo	Patients with idiopathic venous thromboembolism who had received full-dose anticoagulation therapy for a median of 6.5 months	Parallel groups
Agnelli , 2003 n=NA follow-up: 33 months	continuation for 3 or 9 additional months of warfarin or other oral anticoagulant was adjusted to achieve a target INR between 2.0 and 3.0. versus discontinuation (after 3 months)	patients who had had 3 months of oral anticoagulant therapy without experiencing recurrence or bleeding after a first episode of pulmonary embolism	Parallel groups open Italy

continued...

Trial	Treatments	Patients	Trials design and methods
Agnelli , 2001 n=NA follow-up: 33 months	continuation for 9 additional months; warfarin or acenocoumarol adjusted to achieve a target INR between 2.0 and 3.0 versus discontinuation (after 3 months months)	Patients with a first episode of idiopathic proximal deep venous thrombosis who had completed three months of oral anticoagulant therapy	Parallel groups open Italy
LAFIT (Kearon) , 1999 n=NA follow-up:	Continuation of the oral anticoagulant therapy up to 24 months, warfarin was adjusted to achieve a target INR between 2.0 and 3.0. versus discontinuation (after 3 months)	patients who had completed 3 months of anticoagulant therapy for a first episode of idiopathic venous thromboembolism	
ELAET (Kearon) , 2004 n=NA follow-up: 11 months (after randomizatio)	continuation for 2 additionnal months of warfarin adjusted to achieve a target INR between 2.0 and 3.0. versus discontinuation (after 1 months)	-	Parallel groups double blind Canada, US
Levine , 1995 n=NA follow-up: 11 months after randomization.	continuation for 2 months of warfarin adjusted INR value of 2.0 to 3.0 versus Discontinue oral anticoagulant therapy (after 1 months)	Patients with venographically confirmed acute proximal DVT who had received four weeks of warfarin after initial heparin and whose four week IPG was normal	Parallel groups double blind Canada, Italy
DURAC (Schulman) , 1997 n=NA follow-up: Four years after randomization	indefinite warfarin or dicoumarol adjusted for a target INR between 2.0 and 2.85 versus 6 months warfarin or dicoumarol adjusted for a target INR between 2.0 and 2.85	-	Parallel groups open Sweden

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3 extended LMWH

Trial	Treatments	Patients	Trials design and methods
Enoxaparin vs acenocoumarol			
Veiga , 2000 n=50/50 follow-up: 6-9 mo	UFH, APTT 1.52.0d followed by Enoxaparin 4,000 IU qd versus UFH, APTT 1.52.0d followed by Acenocoumarol target INR 2-3	patients with objective diagnosis of DVT by Venography	open
Nadroparin vs acenocoumarol			
Lopez-Beret , 2001 n=81/77 follow-up: 6-9 mo	LMWH, 1,025 IU/10 kg bid followed by Nadroparin 1,025 IU/10 kg bid versus LMWH, 1,025 IU/10 kg bid followed by Acenocoumarol target INR 2-3	patients with objective diagnosis of DVT by compression ultrasonography	open
Lopaciuk , 1999 n=101/101 follow-up: 9 mo	LMWH, 85 UI/kg bid followed by Nadroparin 85 IU/kg qd versus LMWH, 85 UI/kg bid followed by Acenocoumarol target INR 2-3	patients with objective diagnosis of DVT by Venography	open
Tinzaparin vs acenocoumarol			
Romera , 2009 n=119/122 follow-up: 12 months	tinzaparin SC 175 IU anti-Xa per kg once daily for 6 months versus acenocoumarol for target INR 2-3 for 6 months after initial LMWH (until INR 2-3)	patients with symptomatic proximal DVT of the lowerlimbs confirmed by compression duplex ultrasound scan	Parallel groups open Spain
Enoxaparin vs coumarin			
Gonzlez-Fajardo , 2008 n=85/80 follow-up: 1y, 5y	long-term anticoagulant treatment with enoxaparin during at least 3 months versus long-term anticoagulant treatment with coumarin during at least 3 months	patients with symptomatic, unilateral, first-episode DVT	Parallel groups open, blind assessment Spain
Bemiparin vs warfarin			

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Trial	Treatments	Patients	Trials design and methods
Kakkar , 2003 n=221/103 follow-up: 3 mo	LMWH, 115 IU/kg qd followed by Bemiparin 3,500 IU qd versus A: UFH, 30/40,000IU qd; B: LMWH, 115 IU/kg qd followed by Warfarin target INR 2-3	patients with objective diagnosis of DVT by Venography/compression ultrasonography	open
Dalteparin vs warfarin			
Lee , 2003 n=336/336 follow-up: 6 mo	LMWH, 200 IU/kg qd followed by Dalteparin 150 IU/kg qd versus LMWH, 200 IU/kg qd followed by Warfarin target INR 2-3	patients with cancer and objective diagnosis of DVT by Venography/compression ultrasonography	open
Das , 1996 n=50/55 follow-up: 3 mo	UFH followed by Dalteparin 5,000 IU qd versus UFH followed by Warfarin target INR 2-3	patients with objective diagnosis of DVT by Venography	open
Enoxaparin vs warfarin			
Deitcher , 2003 n=51/30 follow-up: 6 mo	LMWH: 1a, 1 mg/kg q12h; 1b, 1 mg/kg qd12h followed by Enoxaparin 1a: 1 mg/kg qd; 1b: 1.5 mg/kg qd versus LMWH, 1 mg/kg q12h followed by Warfarin target INR 2-3	patients with objective diagnosis of DVT	open
Meyer , 2002 n=71/58 follow-up: 3 mo	LMWH, 1.5 mg/kg qd followed by Enoxaparin 1.5 mg/Kg qd versus LMWH, 1.5 mg/kg qd followed by Warfarin target INR 2-3	patients with cancer and objective diagnosis of DVT by Venography/compression ultrasonography	open
Gonzalez-Fajardo , 1999 n=93/92 follow-up: 9 mo	LMWH, 4,000 IU bid followed by Enoxaparin 4,000 IU qd versus UFH followed by Warfarin target INR 2-3	patients with objective diagnosis of DVT by Venography	Parallel groups open
Pini , 1994 n=93/94 follow-up: 9 mo	UFH, APTT 1.31.9 followed by Enoxaparin 4,000 IU qd versus UFH, APTT 1.31.9 followed by Warfarin target INR 2-3.5	patients with objective diagnosis of DVT by Venography (diagnosed by strain-gauge plethysmography plus D-dimer latex assay and confirmed by venography)	open
Tinzaparin vs warfarin			
Hull , 2002 n=369/368 follow-up: 9 mo	LMWH, 175 IU/kg qd followed by Tinzaparin 175 IU/kg qd versus UFH 5 d, followed by UFH therapeutic APTT followed by Warfarin target INR 2-3	patients with objective diagnosis of DVT by Venography/compression ultrasonography	open

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4 home treatment

Trial	Treatments	Patients	Trials design and methods
LMWH at home vs UFH in hospital			
Koopman , 1996 n=202/198 follow-up: 12 weeks	home treatment with twice daily injections of nadroparin at a dose adjusted for patients weight; versus UH (APTT adjusted dose, continuous intravenous infusion of 1250 IU per hour after initial intravenous bolus of 5000 IU) in hospital.	patients with acute symptomatic proximal DVT proven by venography or duplex scan	Parallel groups open The Netherlands, France, Italy, New Zealand Australia
Boccalon , 2000 n=99/101 follow-up: 6 months	home treatment with sub-cutaneous injection of LMWH (dalteparin sodium, enoxaparin sodium or nadroparin calcium as chosen by the attending physician) at the recommended dose followed by anticoagulant for 6 months versus Sub-cutaneous injection of LMWH (dalteparin sodium, enoxaparin sodium or nadroparin calcium as chosen by attending physician) at the recommended dose followed by anticoagulant for 6 months initially in hospital for 10 +/- 2 days then at home	patients with confirmed diagnosis (by ultrasonography or venography) of proximal DVT not more than 30 days before enrolment	Parallel groups NA France
Levine , 1996 n=247/253 follow-up: 90 days	home treatment by Sub-cutaneous enoxaparin 1 mg per kg body weight twice a day for at least 5 days versus UH (APTT adjusted dose, continuous intravenous infusion of 20,000 IU after initial intravenous bolus of 5000 IU) in hospital for at least 5 days	patients with acute proximal DVT proven on venography or duplex scan	Parallel groups open Canada
Ramacciotti , 2004 n=104/97 follow-up:	home treatment by once daily Subcutaneous injection of enoxaparin at a dose of 1.5 mg/kg for 5-10 days versus in hospital intravenous bolus injection of 5000 IU of UFH followed by intravenous 500 IU/kg/day adjusted to maintain an aPTT of 1.5-2.5 times the normal value for 5-10 days.	patients with DVT symptoms for greater than or equal to 10 days and proximal lower limb DVT confirmed by duplex ultrasound or venography	Parallel groups open Brazil

continued...

Trial	Treatments	Patients	Trials design and methods
Daskalopoulos , 2005 n=55/53 follow-up:	home treatment with single sub- cutaneous injection of LMWH (tinzaparin sodium) in a weight adjusted dose (175 anti Xa IU/Kg) daily for 6 months versus Intravenous bolus of 5000IU UFH followed by intravenous infusion of UFH for 5-7 days. APTT was measured after 4 hours of the initiation of heparin administration and was repeated 6 hours thereafter to reach the therapeutic range (ratio: 1.5-2.5). Oral an	patients with acute proximal DVT confirmed by colour duplex UScan not more than 1 week onset	Parallel groups open Greece
Chong , 2005 n=150/148 follow-up: 24 months	once daily sub-cutaneous injection of enoxaparin 1.5mg/kg for a minimum of 5 days plus 10mg of warfarin for 3 months adjusted to achieve INR above 2 and within range accepted by the investigator versus 5000 IU bolus of unfractionated heparin (UFH) for a minimum of 5 days plus 10mg warfarin started on day 1 of the treatment for 3 months	patients with diagnosis of symptomatic lower extremity DVT (proximal or distal) confirmed by either contrast venography and/or ultrasonography, be suitable for treatment in an outpatient setting	Parallel groups open Australia, New Zealand, Poland, South Africa

References

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5 Low molecular weight heparin

Trial	Treatments	Patients	Trials design and methods
Dalteparin vs unfractionated heparin			
Holm et al , 1986 n=29/27 follow-up: Hospital Stay	Dalteparin Subcutaneous twice daily adjusted for 7 Days, 57-107 U/kg BID versus unfractionated heparin subcutaneous twice daily 16000-30000 U	-	
Bratt et al , 1985 n=25/29 follow-up: 23 Months (mean)	Dalteparin Intravenous (adjusted) for >=5 Days, 120 U/kg BID versus unfractionated heparin intravenous APPTx1.7-3.5	-	
Bratt et al , 1990 n=60/60 follow-up: 65279;Hospital stay	Dalteparin Subcutaneous twice daily adjusted for >= 5 Days, 120 U/kg BID versus unfractionated heparin intravenous APPTx2-4	-	
Lindmarker et al , 1993 n=101/103 follow-up: 6 Months	Dalteparin Subcutaneous once daily for >= 5 Days, 200 U/kg BID versus unfractionated heparin intravenous APPTx1.5-3	-	
Enoxaparin vs unfractionated heparin			
Simonneau et al , 1993 n=67/67 follow-up: 3 Months	Enoxaparin Subcutaneous twice daily for 0 Days, 100 U/kg BID versus unfractionated heparin intravenous APPTx1.5-2.5	-	
Minoctoparine vs unfractionated heparin			
Faivre et al , 1988 n=33/37 follow-up: 10 Days	Minoctoparine (CY222) Subcutaneous twice daily for 10 Days,155 U/kg BID versus unfractionated heparin subcutaneous twice daily APPTx2-3	-	
Nadroparin vs unfractionated heparin			
Collaborative European Multicentre , 1991 n=70/66 follow-up: 12 Weeks	Nadroparin Subcutaneous twice daily for 10 Days, 90 U/kg BID versus unfractionated heparin intravenous APPTx1.5-2	-	

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Trial	Treatments	Patients	Trials design and methods
Prandoni et al , 1992 n=85/85 follow-up: 6 Months	Nadroparin Subcutaneous twice daily for >=0 Days, 90 U/kg BID versus unfractionated heparin intravenous APPTx1.5-2	-	
Lopaciuk et al , 1992 n=74/75 follow-up: 3 Months	Nadroparin Subcutaneous twice daily for 10 Days, 92 U/kg BID versus unfractionated heparin subcutaneous twice daily APPTx1.5-2.5	-	
Tinzaparin vs unfractionated heparin			
Hull et al , 1992 n=213/219 follow-up: 3 Months	Tinzaparin Subcutaneous once daily for >= Days, 175 U/kg BID versus unfractionated heparin intravenous APPTx2-3	-	

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6 once daily LMWH

Trial	Treatments	Patients	Trials design and methods
once daily dalteparin vs twice daily dalteparin			
Holmstrm , 1992 n=50/51 follow-up:	once daily dalteparin 200 U (anti-FXa)/kg for at least 5 days versus twice daily dalteparin 100 U (anti-FXa)/kg for at least 5 days	Patients with a first occurrence of DVT in the lower limb, confirmed with phlebography	Parallel groups open Sweden
Partsch , 1996 n=76/64 follow-up:	Fragmin administered 200 IU/kg once daily for at least 7 days versus Fragmin 100 IU/kg twice daily for at least 7 days	patients presented with DVT extending into the iliofemoral segment diagnosed by duplex ultrasonography	Parallel groups NA Austria
once daily enoxaparin vs twice daily enoxaparin			
Merli , 2001 n=298/312 follow-up:	enoxaparin 1.5 mg/kg body weight once daily versus S.c. enoxaparin at fixed dosages of 1.0 mg/kg of body weight twice daily	patients with a symptomatic lower-extremity DVT confirmed by venography or ultrasonography (including patients with confirmed PE)	Parallel groups double blind Europe, United States of America and Australia, image/pj
once daily logiparin vs twice daily logiparin			
Siegbahn , 1989 n=10/10 follow-up:	Once daily logiparin 150 XaI U/kgp, imag versus twice daily logiparin 75 XaI U/kg	patients with a venographically confirmed episode of DVT	Parallel groups single blind Sweden and Denmark
once daily nadroparin vs twice daily nadroparin			
Charbonnier , 1998 n=316/335 follow-up:	Once daily nadroparin 20,500 (AXa IU/ml)continued for at least 5 days versus twice daily nadroparin 10,250 (AXa IU/ml)continued for at least 5 days	patients with acute symptomatic proximal DVT in popliteal vein or above documented by venography	Parallel groups double blind Europe
once daily enoxaparin vs UFH			
Merli (once daily vs UFH) , 2001 n=298/290 follow-up: 3 months	Initial therapy with enoxaparin 1.5 mg/kg body weight once daily versus Initial therapy with dose-adjusted intravenous unfractionated heparin	patients with a symptomatic lower-extremity DVT confirmed by venography or ultrasonography (including patients with confirmed PE)	Parallel groups partially blinded Europe, United States of America and Australia, image/pj

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7 prolonged oral VKA

Trial	Treatments	Patients	Trials design and methods
6 months vs 1.5 months			
Schulman , 1995 n=NA follow-up: Two years after randomization	6 months treatment with warfarin or dicoumarol adjusted for a target INR between 2.0 - 2.85 versus 1.5 months warfarin or dicoumarol adjusted for a target INR between 2.0 - 2.85	-	Parallel groups open Sweden
3-6 months vs 1.5-3 months			
Pinede , 2001 n=NA follow-up: 15 months after randomization	Long course of therapy (6 months for proximal DVT and/or PE; 12 weeks for calf DVT) by fluidione adjusted for INR range of 2.0 to 3.0 versus Short oral anticoagulant course (3 months for proximal DVT and/or PE; 6 weeks for isolated calf DVT) by fluidione adjusted for INR range of 2.0 to 3.0	-	Parallel groups open France

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8 subcutaneous heparin

Trial	Treatments	Patients	Trials design and methods
subcutaneous heparin vs intravenous heparin			
Krahenbuhl , 1979 n=23/25	subcutaneous sodic heparin 30 000 U daily (mean) versus intravenous sodic heparin 30 000 U daily (mean)	-	
Bentley , 1980 n=50/50	subcutaneous calcic heparin 37 000 U daily (mean) versus intravenous sodic heparin 36 800 U daily (mean)	-	
Andersson , 1982 n=72/69	subcutaneous sodic heparin 36 800 U daily (mean) versus intravenous sodic heparin 33 250 U daily (mean)	-	
Hull , 1986 n=57/58	subcutaneous sodic heparin 32 300 U daily (mean) versus intravenous sodic heparin 29 700 U daily (mean)	-	
Doyle , 1987 n=51/52	subcutaneous calcic heparin 29 200 U daily (mean) versus intravenous calcic heparin 29 600 U daily (mean)	-	
Walker , 1987 n=50/50	subcutaneous calcic heparin 29 375 U daily (mean) versus intravenous calcic heparin 24 384 U daily (mean)	-	

continued...

Trial	Treatments	Patients	Trials design and methods
Lopaciuk , 3000 n=48/46	subcutaneous sodic heparin 34 400 U daily (mean) versus intravenous sodic heparin 37 000 U daily (mean)	-	
Pini , 1990 n=138/133	subcutaneous calcic heparin 33 800 U daily (mean) versus intravenous sodic heparin 31 700 U daily (mean)	-	

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9 About TrialResults-center.org

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