

Clinical trials of heparin

TrialResults-center www.trialresultscenter.org

1 venous thrombosis

Trial	Treatments	Patients	Trials design and methods
tPA+heparin vs no fibrinolysis			
Schweizer tPA , 1998 n=NA follow-up:	tPA 20 mg IV into pedal vein over 4 hours each day for 7 days. Heparin IV given concomitantly, with adjustment versus heparin IV, adjusted for 7 days	patients with venographically confirmed DVT of leg duration <7 days.	Parallel groups single blind Germany
heparin+warfarin vs placebo			
Ott import , 1998 n=11/12	anticoagulants (s.c. heparin followed by oral warfarin) (duration NA) versus s.c. saline followed by oral placebo tablets	-	double blind Denmark
heparin/dabigatran vs heparin/VKA			
RE-COVER , 2009 [NCT00291330] n=1274/1265 follow-up: 6 months	dabigatran 150 mg twice daily in a fixed-dose versus warfarin dose-adjusted to an INR between 2.0 and 3.0	patients with acute venous thromboembolism , treated with low molecular weight or unfractionated heparin for 5 to 11 days	Parallel groups double blind
RE-COVER II , 2011 <i>unpublished</i> [NCT00680186] n=1294/1295 follow-up: 6 months	dabigatran, 150 mg twice daily, for 6 months versus warfarin, dose-adjusted to an INR of 2.0 and 3.0, for 6 months	patients with acute VTE, treated with low molecular weight or unfractionated heparin for 5 to 11 days	Parallel groups double-blind 31 countries
heparin/edoxaban vs heparin/VKA			
Edoxaban Hokusai VTE , 2013 [NCT00986154] n=4143/4149 follow-up:	heparin then edoxaban 60mg daily (30mg if creatine clearance of 30 to 50 ml/min or <60kg) for 3 to 12 months versus heparin then warfarin	patients with acute venous thromboembolism, who had initially received heparin,	Parallel groups double-blind
idraparinux (without heparin) vs heparin/VKA			

continued...

Trial	Treatments	Patients	Trials design and methods
VanGogh DVT , 2007 [NCT00067093] n=1452/1452 follow-up: 3 mo (6 mo)	subcutaneous idraparinux (2.5 mg once weekly) versus heparin followed by an adjusted-dose vitamin K antagonist	patients with deep-vein thrombosis	Parallel groups open
VanGogh PE , 2007 [NCT00062803] n=1095/1120 follow-up: 3 mo (6 mo)	subcutaneous idraparinux (2.5 mg once weekly) versus heparin followed by an adjusted-dose vitamin K antagonist	patients with pulmonary embolism	Parallel groups open
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)	-	

continued...

Trial	Treatments	Patients	Trials design and methods
Walker , 1987 n=50/50	subcutaneous calcic heparin 29 375 U daily (mean) versus intravenous calcic heparin 24 384 U daily (mean)	-	
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)	-	
heparin+phenprocoumon vs phenylbutazone			
Nielsen import , 1994 n=48/42	heparin and phenprocoumon for 3 months versus phenylbutazone	-	open Denmark

3

More details and results :

- fibrinolysis for venous thrombosis in all type of patients at <http://www.trialresultscenter.org/go-Q100>
- antithrombotics for venous thrombosis in all type of patients at <http://www.trialresultscenter.org/go-Q101>
- heparin (UFH or LMWH) for venous thrombosis in all type of patients at <http://www.trialresultscenter.org/go-Q204>
- UFH for venous thrombosis in all type of patients at <http://www.trialresultscenter.org/go-Q205>
- direct oral anticoagulant (DAO) for venous thrombosis in all types of patients at <http://www.trialresultscenter.org/go-Q505>

References

Schweizer tPA, 1998:

Schweizer J, Elix H, Altmann E, Hellner G, Forkmann L Comparative results of thrombolysis treatment with rt-PA and urokinase: a pilot study. Vasa 1998;27:167-71 [9747153]

Ott import, 1998:

Ott P, Eldrup E, Oxholm P [Value of anticoagulant therapy in deep venous thrombosis in the lower limb in elderly, mobilized patients. A double-blind placebo controlled study with open therapeutic guidance] Ugeskr Laeger 1988;150:218-21 [3287734]

RE-COVER, 2009:

Schulman S, Eriksson H, Goldhaber SZ, et al. Dabigatran etexilate versus warfarin in the treatment of venous thromboembolism. Oral presentation, ASH Annual Meeting 2009, Abstract number 19394, 6 December 2009

Schulman S, Kearon C, Kakkar AK, Mismetti P, Schellong S, Eriksson H, Baanstra D, Schnee J, Goldhaber SZ Dabigatran versus warfarin in the treatment of acute venous thromboembolism. *N Engl J Med* 2009 Dec 10;361:2342-52 [[19966341](#)] [10.1056/NEJMoa0906598](#)

RE-COVER II, 2011:

unpublished

Schulman S, Kakkar AK, Goldhaber SZ, Schellong S, Eriksson H, Mismetti P, Christiansen AV, Friedman J, Le Maulf F, Peter N, Kearon C Treatment of acute venous thromboembolism with dabigatran or warfarin and pooled analysis. *Circulation* 2014 Feb 18;129:764-72 [[24344086](#)]

Edoxaban Hokusai VTE, 2013:

Edoxaban versus Warfarin for the Treatment of Symptomatic Venous Thromboembolism. *N Engl J Med* 2013 Aug 31;: [[23991658](#)] [10.1056/NEJMoa1306638](#)

VanGogh DVT, 2007:

Buller HR, Cohen AT, Davidson B, Decousus H, Gallus AS, Gent M, Pillion G, Piovella F, Prins MH, Raskob GE *N Engl J Med* 2007 Sep 13;357:1094-104 [[17855670](#)]

VanGogh PE, 2007:

Buller HR, Cohen AT, Davidson B, Decousus H, Gallus AS, Gent M, Pillion G, Piovella F, Prins MH, Raskob GE *N Engl J Med* 2007 Sep 13;357:1094-104 [[17855670](#)]

Krahenbuhl, 1979:

Krahenbuhl B, Simon CA, Bouvier CA, Schinas P, Hopf MA, Cochet B [Heparin treatment. Comparison between intravenous and subcutaneous administration] *Schweiz Med Wochenschr* 1979;109:1322-5 [[504973](#)]

Bentley, 1980:

Bentley PG, Kakkar VV, Scully MF, MacGregor IR, Webb P, Chan P, Jones N An objective study of alternative methods of heparin administration. *Thromb Res* 1980;18:177-87 [[7404497](#)]

Andersson, 1982:

Andersson G, Fagrell B, Holmgren K, Johnsson H, Ljungberg B, Nilsson E, Wilhelmsson S, Zetterquist S Subcutaneous administration of heparin. A randomised comparison with intravenous administration of heparin to patients with deep-vein thrombosis. *Thromb Res* 1982;27:631-9 [[7179208](#)]

Hull, 1986:

Hull RD, Raskob GE, Hirsh J, Jay RM, Leclerc JR, Geerts WH, Rosenbloom D, Sackett DL, Anderson C, Harrison L Continuous intravenous heparin compared with intermittent subcutaneous heparin in the initial treatment of proximal-vein thrombosis. *N Engl J Med* 1986;315:1109-14 [[3531862](#)]

Doyle, 1987:

Doyle DJ, Turpie AG, Hirsh J, Best C, Kinch D, Levine MN, Gent M Adjusted subcutaneous heparin or continuous intravenous heparin in patients with acute deep vein thrombosis. A randomized trial. *Ann Intern Med* 1987;107:441-5 [[3307582](#)]

Walker, 1987:

Walker MG, Shaw JW, Thomson GJ, Cumming JG, Thomas ML Subcutaneous calcium heparin versus intravenous sodium heparin in treatment of established acute deep vein thrombosis of the legs: a multicentre prospective randomised trial. *Br Med J (Clin Res Ed)* 1987;294:1189-92 [[3109574](#)]

Lopaciuk, 3000:**Pini, 1990:**

Pini M, Pattachini C, Quintavalla R, Poli T, Megha A, Tagliaferri A, Manotti C, Dettori AG Subcutaneous vs intravenous heparin in the treatment of deep venous thrombosis—a randomized clinical trial. *Thromb Haemost* 1990;64:222-6 [2270531]

Nielsen import, 1994:

Nielsen HK, Husted SE, Krusell LR, Fasting H, Charles P, Hansen HH Silent pulmonary embolism in patients with deep venous thrombosis. Incidence and fate in a randomized, controlled trial of anticoagulation versus no anticoagulation. *J Intern Med* 1994;235:457-61 [8182402]

Nielsen HK, Husted SE, Krusell LR, Fasting H, Charles P, Hansen HH, Nielsen BO, Petersen JB, Bechgaard P Anticoagulant therapy in deep venous thrombosis. A randomized controlled study. *Thromb Res* 1994;73:215-26 [8191414]

2 pulmonary embolism

Trial	Treatments	Patients	Trials design and methods
idraparinux (without heparin) vs heparin/VKA			
VanGogh PE , 2007 [NCT00062803] n=1095/1120 follow-up: 3 mo (6 mo)	subcutaneous idraparinux (2.5 mg once weekly) versus heparin followed by an adjusted-dose vitamin K antagonist	patients with pulmonary embolism	Parallel groups open

More details and results :

- antithrombotics for pulmonary embolism in all type of patients at <http://www.trialresultscenter.org/go-Q102>

References

VanGogh PE, 2007:

Buller HR, Cohen AT, Davidson B, Decousus H, Gallus AS, Gent M, Pillion G, Piovella F, Prins MH, Raskob GE *N Engl J Med* 2007 Sep 13;357:1094-104 [17855670]

3 superficial thrombophlebitis

Trial	Treatments	Patients	Trials design and methods
heparin vs			
Belcaro (hep vs defibrotide) , 1990 n=NA	-	-	

continued...

Trial	Treatments	Patients	Trials design and methods
heparin spraygel vs clexane			
Gorski , 2005 n=NA follow-up:	Topical liposomal heparin spraygel (4 puffs of 458 IU three times daily) versus clexane (40 mg once daily)	patients with symptomatic superficial venous thrombosis confirmed by ultrasonography with first symptoms not earlier than 72 hours	
liposomal heparin-spraygel vs enoxaparin			
Katzenschlager , 2003 n=NA follow-up:	Topical liposomal heparin-spraygel (lipohep 2400 IU/g, 4 spray puffs three times daily) for 7-14 days versus enoxaparin (40 mg s.c.) for 7-14 days	with ST diagnosed by ultrasound with signs and symptoms lasting less than 72 hours daily)	
heparin vs low dose UFH			
Marchiori , 2002 n=NA follow-up:	UFH (s.c. 12500 IU for one week then 10000 IU) for 4 weeks versus UFH (5000 IU)	patients with ST of the great saphenous vein	
heparin vs no treatment			
Belcaro (hep vs no hep) , 1989 n=NA	-	-	

More details and results :

- antithrombotics for superficial thrombophlebitis in superficial thrombophlebitis of the leg at <http://www.trialresultscenter.org/go-Q218>

References

Belcaro (hep vs defibrotide), 1990:

Gorski, 2005:

Grski G, Szopinski P, Michalak J, Marianowska A, Borkowski M, Geremek M, Trochimczuk M, Brotnek J, Srnk S, Semnka J, Wilkowski D, Noszczyk W Liposomal heparin spray: a new formula in adjunctive treatment of superficial venous thrombosis. *Angiology* 2005;56:9-17 [15678251]

Katzenschlager, 2003:

Marchiori, 2002:

Marchiori A, Verlato F, Sabbion P, Camporese G, Rosso F, Mosena L, Andreozzi GM, Prandoni P High versus low doses of unfractionated heparin for the treatment of superficial thrombophlebitis of the leg. A prospective, controlled, randomized study. *Haematologica* 2002;87:523-7 [12010667]

Belcaro (hep vs no hep), 1989:

Entry terms: dabigatran, Pradaxa, Pradax, idraparinux, idraparinux, , Heparin, Unfractionated Heparin, Heparinic Acid, Liquaemin, Sodium Heparin, Heparin Sodium, alpha-Heparin, alpha Heparin, , edoxaban