Clinical trials of antithrombotics for thrombosis prevention in medical patients

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1 Extended-duration prophylaxis

Trial	Treatments	Patients	Trials design and methods
Extended-duration prophylaxis vs error			
EXCLAIM , 2010 [NCT00077753] n=2975/2988 follow-up: 28 days	Enoxaparin, 40 mg/d subcutaneously (for 28 +/-4 days after receiving openlabel enoxaparin for an initial 10+/-4 days versus placebo for 28 +/-4 days after receiving openlabel enoxaparin for an initial 10+/-4 days.	Acutely Ill Medical Patients With Recently Reduced Mobility	Parallel groups double-blind North and South America
rivaroxaban vs placebo			
MARINER *ongoing* [NCT02111564] n=NA follow-up:	rivaroxaban thromboprophylaxis using rivaroxaban, begun at hospital discharge and continued for 45 days, versus placebo	high-risk medical patients	

References

EXCLAIM, 2010:

Hull RD, Schellong SM, Tapson VF, Monreal M, Samama MM, Nicol P, Vicaut E, Turpie AG, Yusen RD Extended-duration venous thromboembolism prophylaxis in acutely ill medical patients with recently reduced mobility: a randomized trial. Ann Intern Med 2010;153:8-18 [20621900] 10.1059/0003-4819-153-1-201007060-00004

MARINER, :

Raskob GE, Spyropoulos AC, Zrubek J, Ageno W, Albers G, Elliott CG, Halperin J, Haskell L, Hiatt WR, Maynard GA, Peters G, Spiro T, Steg PG, Suh EY, Weitz JI The MARINER trial of rivaroxaban after hospital discharge for medical patients at high risk of VTE. Design, rationale, and clinical implications. Thromb Haemost 2016;115:1240-8 [26842902]

2 low molecular weight heparin

Trial	Treatments	Patients	Trials design and methods
dalteparin vs placebo			
Leizorovicz , 2004 n=1856/1850 follow-up: 21 days	Dalteparin 5000E once daily, 1' days versus placebo	Congestive heart failure (NYHA IIIIV), acute or chronic respiratory disease, infectious and rheumatologic disease	Parallel groups double blind
Enoxaparin vs placebo			

continued...

Trial	Treatments	Patients	Trials design and methods
LIFENOX , 2011 [NCT00622648] n=4171/4136 follow-up: 30 days	subcutaneous enoxaparin 40 mg daily for 104 days versus placebo	hospitalized, acutely ill medical patients	Parallel groups double-blind China, India, Korea, Malaysia, Mexico, the Philippines, and Tunisia
Lederle , 2006 n=140/140 follow-up: 90 days	Enoxaparin 40 mg once daily, until hospital discharge versus placebo	Hospitalization in general medical unit	Parallel groups double blind
MEDENOX , 1999 n=291/288 follow-up: 6-14 days	Enoxaparin 20 mg or 40 mg once daily, 614 days versus placebo	Acute decompensated chronic obstructive pulmonary disease with mechanical ventilation	Parallel groups double blind
Nadroparin vs placebo			
Bergmann , 1996 n=NA follow-up: up to 21	nadroparin 7500 u anti-Xa once daily versus placebo	hospitalized medical	Parallel groups
Fraisse , 2000 n=109/114 follow-up: <=21 days	Nadroparin 38005700E once daily, Until no longer mechanical ventilation, <=21 days versus placebo	Acute decompensated chronic obstructive pulmonary diseasewith mechanical ventilation	Parallel groups double blind
Mahe , 2005 n=1230/1244 follow-up: <=21 days	nadroparin 7500E once daily, Until hospital discharge, <=21 days versus placebo	Congestive heart failure (NYHA IIIIV), acute or respiratory disease, nonpulmonary sepsis, cancer	Parallel groups double blind
Pharmuka vs placebo			
Dahan , 1986 n=132/131 follow-up: <10 days	Pharmuka 60 mg once daily, Until hospital discharge,<=10 days versus placebo	Congestive heart failure (NYHA IIIIV), acute or respiratory infectious disease	Parallel groups double blind
certoparin vs UFH			
CERTIFY , 2010 n=NA	-	-	
dalteparin vs UFH			
PROTECT , 2011 [NCT00182143] n=1873/1873 follow-up:	subcutaneous dalteparin 5000 IU once daily versus unfractionated heparin 5000 IU twice daily	critically ill patients	Parallel groups double-blind Canada, Australia, Brazil, Saudi Arabia, US, UK
enoxaparin vs UFH			
Bergmann and Neuhart , 1996 n=NA follow-up: 10 days	enoxaparin 20 mg once daily for 10 days versus unfractionated heparin (UFH) 5000 IU twice daily	elderly in-patients bedridden for an acute medical illness	Parallel groups double-blind

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Trial	Treatments	Patients	Trials design and methods
Lechler , 1996 n=NA follow-up: 7 days	enoxaparin 40 mg versus unfractionated heparin (Ca-heparin), 3 x 5,000 U)	hospitalized medical patients	Parallel groups double-blind
Kleber , 2003 n=NA follow-up: 10 +/- 2 days	enoxaparin 40 mg once daily for 10 +/2 days versus UFH 5000 IU 3 times daily for 10 +/2 days	severe respiratory disease or heart failure	Parallel groups open Germany
LMWH vs UFH			
Harenberg , 1990 n=NA follow-up: 10 days	1 x 1.500 aPTT units of a LMW heparin fraction versus 3 x 5.000 IU of an unfractionated heparin	patients aged 40-80 years	Parallel groups double-blind
Harenberg , 1996 n=NA follow-up: 10 days	1 daily subcutaneous administration of LMW heparin for 10 days versus 3 x 5,000 IU unfractionated (UF) heparin for 10 days	medical inpatients	Parallel groups double-blind

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Leizorovicz A, Cohen AT, Turpie AG, Olsson CG, Vaitkus PT, Goldhaber SZ Randomized, placebo-controlled trial of dalteparin for the prevention of venous thromboembolism in acutely ill medical patients. Circulation 2004;110:874-9 [15289368]

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Riess H, Haas S, Tebbe U, Gerlach HE, Abletshauser C, Sieder C, Rossol S, Pfeiffer B, Schellong SM A randomized, double-blind study of certoparin vs. unfractionated heparin to prevent venous thromboembolic events in acutely ill, non-surgical patients: CERTIFY Study. J Thromb Haemost 2010;8:1209-15 [20218984] 10.1111/j.1538-7836.2010.03848.x

PROTECT, 2011:

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3 NOAC

Trial	Treatments	Patients	Trials design and methods
apixaban vs enoxaparin			
ADOPT , 2011 [NCT00457002] n=3255/3273 follow-up: 30 days	apixaban, administered orally at a dose of 2.5 mg twice daily for 30 days versus enoxaparin, administered subcutaneously at a dose of 40 mg once daily for 6 to 14 days	acutely ill patients who had congestive heart failure or respiratory failure or other medical disorders and at least one additional risk factor for venous thromboembolism and who were hospitalized with an expected stay of at least 3 days	double-blind
betrixaban vs enoxaparin			
APEX , 2016 [NCT01583218] n=3759/3754 follow-up:	betrixaban (at a dose of 80 mg once daily) for 35 to 42 days versus subcutaneous enoxaparin (at a dose of 40 mg once daily) for 104 days	-	Parallel groups double-blind

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4 platelet aggregation inhibitors

Trial	Treatments	Patients	Trials design and methods
aspirin + dipyridamol vs control			
Chicago , 1982 n=12/15 follow-up:	aspirin, 300 mg bid, and dipyridamole, 75 mg tid versus control	patients with acute spinal cord injury	Parallel groups open
aspirin + dipyridamol vs placebo			
Frankfurt , 1981 *unpublished* n=25/14 follow-up:	A+Dip,A1320 versus placebo	patients with myocardial infarction	Parallel groups double-blind
dipyridamol + ASA vs placebo			
Denver-II , 1980 n=19/19 follow-up: 18 months	dipyridamole 100 mg a day and aspirin 1200 mg a day versus placebo	patients with recurring venous thromboembolism	Parallel groups double-blind
ticlopidine vs placebo			
McKenna-II , 1983 *unpublished* n=27/26 follow-up:	Ticlopidine versus placebo	high risk (post CVA) medical patients	Parallel groups double-blind

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5 synthetic oligosaccharide

Trial	Treatments	Patients	Trials design and methods
fondaparinux vs placebo			
ARTEMIS (Cohen) , 2006 n=425/414 follow-up: 6-15 days	Fondaparinux 2.5 mg once daily for 614 days versus placebo	High-risk medical patients	Parallel groups double blind 8 countries
fondaparinux vs enoxaparin			
BRiEF [NCT00521885] n=NA follow-up:	fondaparinux 2.5mg qd versus enoxaparin 40mg qd	acute medically ill, non-surgical patients	Parallel groups Germany

References

ARTEMIS (Cohen), 2006:

Cohen AT, Davidson BL, Gallus AS, Lassen MR, Prins MH, Tomkowski W, Turpie AG, Egberts JF, Lensing AW Efficacy and safety of fondaparinux for the prevention of venous thromboembolism in older acute medical patients: randomised placebo controlled trial. BMJ 2006;332:325-9 [16439370]

BRiEF, :

6 unfractionated heparin

Trial	Treatments	Patients	Trials design and methods
UFH vs control			
Blech , 1981 n=50/50 follow-up: <=14 days	Unfractionated heparin, 5000 U trice daily, until mobilized versus control	Heart failure, chest infection	Parallel groups open
Cade n=NA follow-up: <=10 days	-	Age >40, complete bed rest, cardiac failure, obesity, previous VTE, cancer or recent surgery	Parallel groups
Gardlund , 1996 n=5776/5917 follow-up: <=60 days	Unfractionated heparin, 5000 U twice daily, until hospital discharge, <=21 days versus control	Age >55, infectious disease Immobilization	Parallel groups open

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7 About TrialResults-center.org

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