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 , 2018 [NCT02111564] n=6007/6012 follow-up:	once-daily rivaroxaban at a dose of 10 mg (with the dose adjusted for renal insufficiency) , begun at hospital discharge and continued for 45 days versus placebo	high-risk medical patients : medically ill patients who were at increasedrisk for venous thromboembolism on the basis of a modified International Medical Prevention Registry on Venous Thromboembolism (IMPROVE) score of 4 or higher (scores range from 0 to 10, with higher scores indicating a higher risk of venous thromboembolism) or a score of 2 or 3 plus a plasma d-dimer level of more than twice the upper limit of the normal range (defined according to local laboratory criteria)	double blind

References

EXCLAIM, 2010:

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MARINER, 2018:

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]

Spyropoulos AC Rivaroxaban for Thromboprophylaxis after Hospitalization for Medical Illness. N Engl J Med 2018;379:1118-1127 [30145946] 10.1056/NEJMoa1805090

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			
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			

continued...

Trial	Treatments	Patients	Trials design and methods
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
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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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	Patients who were hospitalized for acute medical illnesses and with an elevated d-dimer level	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:

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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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