

Clinical trials of antithrombotics for DVT prophylaxis 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 <i>ongoing</i> [NCT02111564] n=NA follow-up: | rivaroxaban thromboprophylaxis using rivaroxaban, begun at hospital discharge and continued for 45 days, versus placebo | high-risk medical patients | |

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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 |
| Samama , 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 |

continued...

| 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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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 | - | double-blind |
| rivaroxaban vs enoxaparin | | | |

continued...

| Trial | Treatments | Patients | Trials design and methods |
|--|---|---|---------------------------------|
| MAGELLAN , 2011 <i>unpublished</i> [NCT00571649] n=4050/4051 follow-up: 35 days | rivaroxaban 10 mg once daily for 35 days versus subcutaneous enoxaparin 40 mg once daily for 10 days | patients hospitalized for acute medical illness | Parallel groups double-blind |

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5

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 <i>unpublished</i> n=25/14 follow-up: | A+Dip,A1320 versus placebo | patients with myocardial infarction | Parallel groups double-blind |
| error vs placebo | | | |
| Denver-I n=14/14 | SP versus placebo | High risk medical patients | |
| 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 |

continued...

| Trial | Treatments | Patients | Trials design and methods |
|---|----------------------------------|---|----------------------------------|
| Toulouse-II <i>unpublished</i> n=40/40 follow-up: | A990+Dip versus placebo | patients with stroke | Parallel groups double-blind |
| Den Ottolander , 1982 n=14/14 follow-up: | A1500+RA233 versus placebo | patients with decompensated heart disease | |
| GRAND , 1987 <i>unpublished</i> n=63/64 follow-up: | GR32191B versus placebo | High risk medical patients | |
| Jones , 1987 <i>unpublished</i> n=60/60 follow-up: | Dazoxidben versus placebo | High risk medical patients | |
| ticlopidine vs placebo | | | |
| McKenna-II , 1983 <i>unpublished</i> 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 |

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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

TrialResults-center is an innovative knowledge database that collects the results of RCTs and provides dynamic interactive systematic reviews and meta-analysis in the field of all major heart and vessels diseases.

The TrialResults-center database provides a unique view of the treatment efficacy based on all data provided directly from clinical trial results, offering a valuable alternative to personal bibliographic search, published meta-analysis, etc. Furthermore, it would allow comparing easily the various concurrent therapeutic for the same clinical condition.

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