

# Clinical trials of antithrombotics for pulmonary embolism in all type of patients

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## 1 anticoagulant

Trial	Treatments	Patients	Trials design and methods
<b>anticoagulant vs no anticoagulant</b>			
<b>BARRIT , 1960</b> n=16/19 follow-up:	heparin IV 10000 UI every 6 hours for 6 doses, nicoumalone ajusted for prothrombin time between 2-3x control versus no anticoagulant	patients with pulmonary embolism	Parallel groups open

## References

### BARRIT, 1960:

BARRITT DW, JORDAN SC Anticoagulant drugs in the treatment of pulmonary embolism. A controlled trial. Lancet 1960 Jun 18;1:1309-12 [[13797091](#)]

## 2 direct anti-Xa

Trial	Treatments	Patients	Trials design and methods
<b>apixaban 2.5mg vs discontinuation</b>			
<b>AMPLIFY-EXT 2.5mg , 2012</b> [NCT00633893] n=842/829 follow-up: 12 mo	Extended Treatment with apixaban 2.5 mg twice daily 12 months versus placebo	patients who have completed their intended treatment for deep vein thrombosis or pulmonary embolism	Parallel groups double blind
<b>apixaban 5mg vs discontinuation</b>			
<b>AMPLIFY-EXT 5mg , 2012</b> [NCT00633893] n=815/829 follow-up: 12 mo	Extended Treatment with apixaban 5 mg twice daily 12 months versus placebo	patients who have completed their intended treatment for deep vein thrombosis or pulmonary embolism	double blind
<b>apixaban (without LMWH) vs LMWH/VKA</b>			
<b>AMPLIFY , 2013</b> [NCT00643201] n=2691/2704 follow-up: 6 mo	apixaban 10 mg twice daily for 7 days then 5 mg, twice daily, 6 months versus conventional therapy: enoxaparin 1mg/kg twice daily until INR $\geq$ 2 then warfarin for an INR between 2-4, once daikly, 6 months	patients with deep vein thrombosis or pulmonary embolism	Parallel groups double blind
<b>rivaroxaban (without LMWH) vs LMWH/VKA</b>			

continued...

Trial	Treatments	Patients	Trials design and methods
<a href="#">Einstein-PE Evaluation , 2012</a> [NCT00439777] n=2419/2413 follow-up: 9.8 months	rivaroxaban (15 mg twice daily for 3 weeks, followed by 20 mg once daily) for 3, 6, or 12 months versus standard therapy with enoxaparin followed by an adjusted-dose vitamin K antagonist	patients who had acute symptomatic pulmonary embolism with or without deep-vein thrombosis	Parallel groups open 38 countries

## References

### AMPLIFY-EXT 2.5mg, 2012:

Agnelli G, Buller HR, Cohen A, Curto M, Gallus AS, Johnson M, Porcari A, Raskob GE, Weitz JI Apixaban for Extended Treatment of Venous Thromboembolism. N Engl J Med 2012 Dec 8;: [23216615] [10.1056/NEJMoa1207541](#)

### AMPLIFY-EXT 5mg, 2012:

Agnelli G, Buller HR, Cohen A, Curto M, Gallus AS, Johnson M, Porcari A, Raskob GE, Weitz JI Apixaban for Extended Treatment of Venous Thromboembolism. N Engl J Med 2012 Dec 8;: [23216615] [10.1056/NEJMoa1207541](#)

### AMPLIFY, 2013:

Agnelli G, Buller HR, Cohen A, Curto M, Gallus AS, Johnson M, Masiukiewicz U, Pak R, Thompson J, Raskob GE, Weitz JI Oral apixaban for the treatment of acute venous thromboembolism. N Engl J Med 2013 Aug 29;369:799-808 [23808982] [10.1056/NEJMoa1302507](#)

### Einstein-PE Evaluation, 2012:

Oral Rivaroxaban for the Treatment of Symptomatic Pulmonary Embolism. N Engl J Med 2012 Mar 26;: [22449293] [10.1056/NEJMoa1113572](#)

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## 3 low molecular weight heparin

Trial	Treatments	Patients	Trials design and methods
<b>Certoparin vs unfractionated heparin</b>			
<a href="#">Certoparin-Study Group sub group , 1998</a> n=39/41 follow-up: 6 mo	Certoparin, 8000 IU twice daily, 14 days versus Unfractionated heparin: bolus 5000 IU, infusion 20 IU/kg per hour	Symptomatic PE	Parallel groups open
<b>Dalteparin vs unfractionated heparin</b>			
<a href="#">Kuijer , 1995</a> n=32/35 follow-up: 3 mo	Dalteparin, 120 IU/kg twice daily, 5 days versus Unfractionated heparin: bolus 5000 IU, infusion 1250 IU/h	Symptomatic PE	Parallel groups open
<a href="#">Meyer , 1995</a> n=29/31 follow-up: 3 mo	Dalteparin, 120 IU/kg twice daily, 10 days versus Unfractionated heparin: no bolus, infusion 500 IU/kg per day	Symptomatic PE	Parallel groups open
<b>Enoxaparin vs unfractionated heparin</b>			

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>PREPIC , 1998</b> n=41/54 follow-up: 2 y	Enoxaparin, 1 mg/kg twice daily, 8-12 days versus Unfractionated heparin: bolus 5000 IU, infusion 500 IU/kg per day	patients with proximal deep-vein thrombosis who were at risk for pulmonary embolism	Factorial plan open
<b>Merli sub group , 2001</b> n=199/88 follow-up: 3 mo	Enoxaparin, 1mg/kg twice daily or 1.5 mg/kg once daily, 5 days versus Unfractionated heparin: according nomogram at local institution	patients with confirmed pulmonary embolism	Parallel groups open 16 countries
<b>Nadroparin vs unfractionated heparin</b>			
<b>European multicentre study , 1991</b> n=61/47 follow-up: 3 mo	Nadroparin, 47506650 antifactor Xa IU twice daily, 10 days versus Unfractionated heparin: no bolus, infusion, 20 IU/kg per hour	Symptomatic proximal DVT	Parallel groups open (blind assessment) Europe
<b>Prandoni sub-group , 1992</b> n=45/46 follow-up: 6 mo	Nadroparin, 47506650 antifactor Xa IU twice daily, 10 days versus Unfractionated heparin: bolus 100 IU/kg, infusion 35 000 IU/d	Symptomatic proximal DVT	Parallel groups open
<b>Thery , 1992</b> n=35/33 follow-up: 14 d	Nadroparin, 76 IU/kg twice daily, 14 days versus Unfractionated heparin: bolus 50 IU/kg, infusion 600 IU/kg per day	patients with submassive pulmonary embolism	Parallel groups open
<b>Reviparin vs unfractionated heparin</b>			
<b>COLOMBUS sub group , 1997</b> n=138/133 follow-up: 3 mo	Reviparin, 35006300 IU twice daily, 5 days versus Unfractionated heparin: bolus 5000 IU, infusion 1250 IU/h	patients with symptomatic DVT and associated pulmonary embolism	Parallel groups open
<b>Tinzaparin vs unfractionated heparin</b>			
<b>ACTSG (Hull) sub-group , 1992</b> n=97/103 follow-up: 3mo	Tinzaparin, 175 IU/kg once daily, 6 days versus Unfractionated heparin: bolus 5000 IU, infusion 29 76040 320 IU/d	patients with objectively documented PE and underlying proximal deep vein thrombosi	Parallel groups double blind US, Canada
<b>THESEE , 1997</b> n=301/307 follow-up: 3 mo	Tinzaparin, 175 IU/kg once daily, 5 days versus Unfractionated heparin: bolus 50 IU/kg, infusion 500 IU/kg per day	patients with symptomatic pulmonary embolism	Parallel groups open
<b>Campbell , 1998</b> n=6/10 follow-up: 3 mo	Tinzaparin, 175 IU/kg once daily, 5 days versus Unfractionated heparin: bolus 5000 IU, infusion 1400 IU/h	Symptomatic PE	Parallel groups open

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**Certoparin-Study Group sub group, 1998:**

Kirchmaier CM, Wolf H, Schfer H, Ehlers B, Breddin HK Efficacy of a low molecular weight heparin administered intravenously or subcutaneously in comparison with intravenous unfractionated heparin in the treatment of deep venous thrombosis. Certoparin-Study Group. *Int Angiol* 1998;17:135-45 [[9821025](#)]

**Kuijer, 1995:**

Kuijer PM, Gallus AS, Cade JE, Buller HR. /jpeg Randomized comparison of LMWH versus standard heparin in the initial treatment of pulmonary embolism [Abstract]. *ocumen Thromb Haemost.* 1995;73:974

**Meyer, 1995:**

Meyer G, Brenot F, Pacouret G, Simonneau G, Gillet Juvin K, Charbonnier B, Sors H Subcutaneous low-molecular-weight heparin fragmin versus intravenous unfractionated heparin in the treatment of acute non massive pulmonary embolism: an open randomized pilot study. *Thromb Haemost* 1995;74:1432-5 [[8772215](#)]

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**Merli sub group, 2001:**

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Prandoni P, Carnovali M, Marchiori A Subcutaneous adjusted-dose unfractionated heparin vs fixed-dose low-molecular-weight heparin in the initial treatment of venous thromboembolism. *Arch Intern Med* 2004;164:1077-83 [[15159264](#)]

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**COLOMBUS sub group, 1997:**

Low-molecular-weight heparin in the treatment of patients with venous thromboembolism. The Columbus Investigators. *N Engl J Med* 1997;337:657-62 [[9280815](#)]

**ACTSG (Hull) sub-group, 1992:**

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Simonneau G, Sors H, Charbonnier B, Page Y, Laaban JP, Azarian R, Laurent M, Hirsch JL, Ferrari E, Bosson JL, Mottier D, Beau B A comparison of low-molecular-weight heparin with unfractionated heparin for acute pulmonary embolism. The THESEE Study Group. Tinzaparine ou Heparine Standard: Evaluations dans l'Embolie Pulmonaire. *N Engl J Med* 1997;337:663-9 [[9278462](#)]

**Campbell, 1998:**

Campbell IA, Yeoh J, Medlicott S.p, imag Duration of hospital stay in patients with pulmonary venous thromboembolism: a randomised comparison of unfractionated heparin versus low molecular weight heparin [Abstract] *Thorax.* 1998;53: 254

## 4 outpatient treatment

Trial	Treatments	Patients	Trials design and methods
<b>outpatient treatment vs inpatient treatment</b>			
<b>OTPE (Aujesky) , 2011</b> [NCT00425542] n=171/168 follow-up: 90 days	initial outpatient treatment with subcutaneous enoxaparin (5 days) followed by oral anticoagulation (90 days). versus inpatient treatment with subcutaneous enoxaparin (5 days) followed by oral anticoagulation (90 days)	patients with acute, symptomatic pulmonary embolism and a low risk of death (pulmonary embolism severity index risk classes I or II)	Parallel groups open-label Switzerland, France, Belgium, and the USA
<b>Otero , 2010</b> [NCT00214929] n=72/60 follow-up: 3 months	early discharge versus standard hospitalization	low-risk patients with acute symptomatic PE	Parallel groups open-label Spain

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Otero R, Uresandi F, Jimnez D, Cabezudo MA, Oribe M, Nauffal D, Conget F, Rodriguez C, Cayuela A Home treatment in pulmonary embolism. *Thromb Res* 2010;126:e1-5 [19853892] [10.1016/j.thromres.2009.09.026](https://doi.org/10.1016/j.thromres.2009.09.026)

## 5 reversible longlasting indirect inhibitor of activated factor X

Trial	Treatments	Patients	Trials design and methods
<b>idrabiotaparinux vs warfarin</b>			
<b>CASSIOPEA , 2012</b> [NCT00345618] n=1599/1603 follow-up: 99 days	subcutaneous idrabiotaparinux (starting dose 30 mg) after 5-10 days' enoxaparin 10 mg/kg twice daily for at least 3 months or 6 months dependent on clinical presentation versus adjusted-dose warfarin (target INR 2-3) after 5-10 days' enoxaparin 10 mg/kg twice daily	adults with objectively documented acute symptomatic pulmonary embolism	Parallel groups double-blind 37 countries

## References

### CASSIOPEA, 2012:

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pulmonary embolism: a randomised, double-blind, double-dummy, non-inferiority trial. Lancet 2012;379:123-9 [22130488] 10.1016/S0140-6736(11)61505-5

## 6 synthetic oligosaccharide

Trial	Treatments	Patients	Trials design and methods
<b>fondaparinux vs heparin</b>			
MATISSE PE , 2003 n=1103/1110 follow-up: 3 mo	fondaparinux subcutaneously once daily versus continuous intravenous infusion of unfractionated heparin	patients with acute symptomatic pulmonary embolism	Parallel groups open
<b>idraparinux (without heparin) vs heparin/VKA</b>			
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

## References

### MATISSE PE, 2003:

Biller HR, Davidson BL, Decousus H, Gallus A, Gent M, Piovella F, Prins MH, Raskob G, van den Berg-Segers AE, Cariou R, Leeuwenkamp O, Lensing AW Subcutaneous fondaparinux versus intravenous unfractionated heparin in the initial treatment of pulmonary embolism. N Engl J Med 2003 Oct 30;349:1695-702 [14585937]

### VanGogh PE, 2007:

## 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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