

# Clinical trials of anticoagulant for percutaneous coronary intervention in all type of patients

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## 1 direct thrombin inhibitor

Trial	Treatments	Patients	Trials design and methods
<b>bivalirudin vs heparin + GP2b3a inhibitors</b>			
<b>ACUITY (Stone) (bivalirudin alone) , 2006</b> [NCT00093158] n=9216/4603 follow-up: 30 days	bivalirudin alone versus unfractionated heparin or enoxaparin plus a glycoprotein IIb/IIIa inhibitor	patients with acute coronary syndromes	Parallel groups open
<b>HORIZONS-AMI (Stone) , 2008</b> [NCT00433966] n=1800/1802 follow-up: 30 days	Bivalirudin versus Heparin plus GP IIb/IIIa inhibitor	patients with ST-segment elevation myocardial infarction who presented within 12 hours after the onset of symptoms and who were undergoing primary PCI	Parallel groups open 11 countries
<b>REPLACE-2 , 2003</b> n=2994/3008 follow-up: 30 days	bivalirudin, with glycoprotein IIb/IIIa (Gp IIb/IIIa) inhibition on a provisional basis for complications during PCI versus heparin plus planned Gp IIb/IIIa blockade	patients undergoing urgent or elective PCI	Parallel groups double blind 9 countries
<b>bivalirudin + eptifibatide vs heparin + GP2b3a inhibitors</b>			
<b>Kleiman , 2002</b> n=NA follow-up:	bivalirudin + eptifibatide versus heparin + eptifibatide	patients who underwent elective percutaneous coronary intervention	Parallel groups open
<b>bivalirudin vs UFH</b>			
<b>ARMYDA BIVALVE</b> n=140 follow-up:	bivalirudin (0.75 mg/kg bolus followed by 1.75 mg/kg per hour during the procedure) versus unfractionated heparin (75 IU/kg)	patients at high bleeding risk (over 75 years of age, diabetes, reduced renal function) scheduled for PCI	Parallel groups
<b>BAT (Bittl) , 1995</b> n=2059/2039 follow-up: hospital stay	bivalirudin immediately before angioplasty. versus heparin immediately before angioplasty	patients undergoing urgent angioplasty for unstable or postinfarction angina	Parallel groups double blind US
<b>ISAR-REACT 3 , 2008</b> [NCT00262054] n=2289/2281 follow-up: 30 days (mean)	UFH bolus of 140 U/kg versus bivalirudin (bolus of 0.75 mg/kg, followed by infusion of 1.75 mg/kg/hr)	troponin-negative patients undergoing PCI	Parallel groups double blind

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>REPLACE-1 , 2004</b> n=532/524 follow-up: hospital stay (48h min)	bivalirudin (0.75 mg/kg bolus, 1.75 mg/kg/h infusion during the procedure versus heparin (70 U/kg initial bolus) adjusted to ACT of 200 to 300s	patients undergoing elective or urgent revascularization	Parallel groups US
<b>bivalirudin vs UFH plus tirofiban</b>			
<b>NAPLES (Tavano) , 2009</b> n=167/168 follow-up: 30 days	bivalirudin monotherapy versus unfractionated heparin plus tirofiban	patients with diabetes mellitus undergoing elective percutaneous coronary intervention	Parallel groups open Italy

## References

### **ACUITY (Stone) (bivalirudin alone), 2006:**

Stone GW, McLaurin BT, Cox DA, Bertrand ME, Lincoff AM, Moses JW, White HD, Pocock SJ, Ware JH, Feit F, Colombo A, Aylward PE, Cequier AR, Darius H, Desmet W, Ebrahimi R, Hamon M, Rasmussen LH, Rupprecht HJ, Hoekstra J, Mehran R, Ohman EM, , Bivalirudin for patients with acute coronary syndromes. *N Engl J Med* 2006;355:2203-16. [17124018] [10.1056/NEJMoa062437](https://doi.org/10.1056/NEJMoa062437)

### **HORIZONS-AMI (Stone), 2008:**

Mehran R, Brodie B, Cox DA, Grines CL, Rutherford B, Bhatt DL, Dangas G, Feit F, Ohman EM, Parise H, Fahy M, Lansky AJ, Stone GW, The Harmonizing Outcomes with Revascularization and Stents in Acute Myocardial Infarction (HORIZONS-AMI) Trial: study design and rationale. *Am Heart J* 2008;156:44-56. [18585496] [10.1016/j.ahj.2008.02.008](https://doi.org/10.1016/j.ahj.2008.02.008)

Stone GW, Witzenbichler B, Guagliumi G, Peruga JZ, Brodie BR, Dudek D, Kornowski R, Hartmann F, Gersh BJ, Pocock SJ, Dangas G, Wong SC, Kirtane AJ, Parise H, Mehran R Bivalirudin during primary PCI in acute myocardial infarction. *N Engl J Med* 2008 May 22;358:2218-30 [18499566]

Stone GW, Witzenbichler B, Guagliumi G, Peruga JZ, Brodie BR, Dudek D, Kornowski R, Hartmann F, Gersh BJ, Pocock SJ, Dangas G, Wong SC, Fahy M, Parise H, Mehran R Heparin plus a glycoprotein IIb/IIIa inhibitor versus bivalirudin monotherapy and paclitaxel-eluting stents versus bare-metal stents in acute myocardial infarction (HORIZONS-AMI): final 3-year results from a multicentre, randomised controlled trial. *Lancet* 2011 Jun 25;377:2193-2204 [21665265] [10.1016/S0140-6736\(11\)60764-2](https://doi.org/10.1016/S0140-6736(11)60764-2)

### **REPLACE-2, 2003:**

Gibson CM, Ten Y, Murphy SA, Ciaglio LN, Southard MC, Lincoff AM, Waksman R, Association of prerandomization anticoagulant switching with bleeding in the setting of percutaneous coronary intervention (A REPLACE-2 analysis). *Am J Cardiol* 2007;99:1687-90. [17560876] [10.1016/j.amjcard.2007.01.053](https://doi.org/10.1016/j.amjcard.2007.01.053)

Cohen DJ, Lincoff AM, Lavelle TA, Chen HL, Bakhai A, Berezin RH, Jackman D, Sarembock IJ, Topol EJ, Economic evaluation of bivalirudin with provisional glycoprotein IIb/IIIa inhibition versus heparin with routine glycoprotein IIb/IIIa inhibition for percutaneous coronary intervention: results from the REPLACE-2 trial. *J Am Coll Cardiol* 2004;44:1792-800. [15519009] [10.1016/j.jacc.2004.05.085](https://doi.org/10.1016/j.jacc.2004.05.085)

Lincoff AM, Kleiman NS, Kereiakes DJ, Feit F, Bittl JA, Jackman JD, Sarembock IJ, Cohen DJ, Spriggs D, Ebrahimi R, Keren G, Carr J, Cohen EA, Betriu A, Desmet W, Rutsch W, Wilcox RG, de Feyter PJ, Vahanian A, Topol EJ, , Long-term efficacy of bivalirudin and provisional glycoprotein IIb/IIIa blockade vs heparin and planned glycoprotein IIb/IIIa blockade during percutaneous coronary revascularization: REPLACE-2 randomized trial. *JAMA* 2004;292:696-703. [15304466] [10.1001/jama.292.6.696](https://doi.org/10.1001/jama.292.6.696)

Lincoff AM, Bittl JA, Harrington RA, Feit F, Kleiman NS, Jackman JD, Sarembock IJ, Cohen DJ, Spriggs D, Ebrahimi R, Keren G, Carr J, Cohen EA, Betriu A, Desmet W, Kereiakes DJ, Rutsch W, Wilcox RG, de Feyter PJ, Vahanian A, Topol EJ Bivalirudin and provisional glycoprotein IIb/IIIa blockade compared with heparin and planned glycoprotein IIb/IIIa blockade during percutaneous coronary intervention: REPLACE-2 randomized trial. *JAMA* 2003 Feb 19;289:853-63 [12588269]

### **Kleiman, 2002:**

Kleiman NS, Klem J, Fernandes LS, Rubin H, Challa S, Solomon S, Maresh K, Arora U, Klem E, Buergler J, Mathew S, Browning A, DeLao T, Pharmacodynamic profile of the direct thrombin antagonist bivalirudin given in combination with the glycoprotein IIb/IIIa antagonist eptifibatide. *Am Heart J* 2002;143:585-93. [11923794]

### **ARMYDA BIVALVE, :**

### **BAT (Bittl), 1995:**

Bittl JA, Feit F, A randomized comparison of bivalirudin and heparin in patients undergoing coronary angioplasty for postinfarction angina. Hirulog Angioplasty Study Investigators. Am J Cardiol 1998;82:43P-49P. [9809891]

Shah PB, Ahmed WH, Ganz P, Bittl JA, Bivalirudin compared with heparin during coronary angioplasty for thrombus-containing lesions. J Am Coll Cardiol 1997;30:1264-9. [9350925]

Bittl JA, Strony J, Brinker JA, Ahmed WH, Meckel CR, Chaitman BR, Maraganore J, Deutsch E, Adelman B, Treatment with bivalirudin (Hirulog) as compared with heparin during coronary angioplasty for unstable or postinfarction angina. Hirulog Angioplasty Study Investigators. N Engl J Med 1995;333:764-9. [7643883]

Bittl JA, Comparative safety profiles of hirulog and heparin in patients undergoing coronary angioplasty. The Hirulog Angioplasty Study Investigators. Am Heart J 1995;130:658-65. [7668214]

Bittl JA, Chaitman BR, Feit F, Kimball W, Topol EJ Bivalirudin versus heparin during coronary angioplasty for unstable or postinfarction angina: Final report reanalysis of the Bivalirudin Angioplasty Study. Am Heart J 2001;142:952-9 [11717596]

**ISAR-REACT 3, 2008:**

Kastrati A, Neumann FJ, Mehilli J, Byrne RA, Iijima R, Bttner HJ, Khattab AA, Schulz S, Blankenship JC, Pache J, Minners J, Seyfarth M, Graf I, Skelding KA, Dirschinger J, Richardt G, Berger PB, Schmig A Bivalirudin versus Unfractionated Heparin during Percutaneous Coronary Intervention. N Engl J Med 2008 Aug 14;359:688-696 [18703471]

**REPLACE-1, 2004:**

Lincoff AM, Bittl JA, Kleiman NS, Sarembock IJ, Jackman JD, Mehta S, Tannenbaum MA, Niederman AL, Bachinsky WB, Tift-Mann J, Parker HG, Kereiakes DJ, Harrington RA, Feit F, Maieron ES, Chew DP, Topol EJ, , Comparison of bivalirudin versus heparin during percutaneous coronary intervention (the Randomized Evaluation of PCI Linking Angiomax to Reduced Clinical Events [REPLACE]-1 trial). Am J Cardiol 2004;93:1092-6. [15110198] 10.1016/j.amjcard.2004.01.033

**NAPLES (Tavano), 2009:**

Tavano D, Visconti G, D'Andrea D, Focaccio A, Golia B, Librera M, Caccavale M, Ricciarelli B, Briguori C Comparison of bivalirudin monotherapy versus unfractionated heparin plus tirofiban in patients with diabetes mellitus undergoing elective percutaneous coronary intervention. Am J Cardiol 2009;104:1222-8 [19840566]

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## 2 fondaparinux

Trial	Treatments	Patients	Trials design and methods
<b>fondaparinux vs unfractionated heparin or bivalirudin</b>			
<b>SWITCH III</b> <i>ongoing</i> [NCT00464087] n=NA follow-up:	fondaparinux versus unfractionated heparin or bivalirudin	patients experiencing acute coronary syndrome undergoing percutaneous coronary angioplasty	Parallel groups open

### References

SWITCH III, :

## 3 Low Molecular Weight Heparin

Trial	Treatments	Patients	Trials design and methods
<b>dalteparin vs UFH</b>			

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<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
Natarajan (without antiGp2b3a) , 2003 n=NA follow-up:	Dalteparin 100 IU/kg bolus versus UFH 100 IU/kg bolus	Elective or urgent PCI	
<b>enoxaparin vs UFH</b>			
ATOLL , 2010 n=450/460 follow-up: 30 days	IV enoxaparin versus UFH	patients undergoing PCI for acute STEMI	Parallel groups open Austria, France, Germany, and US
Brieger n=346/234 follow-up:	enoxaparin versus unfractionated heparin	patients undergoing percutaneous coronary intervention for ST-segment elevation myocardial infarction (STEMI)	
CRUISE , 2003 n=129/132 follow-up: 2,7 +30 days	Enoxaparin 0.75 mg/kg bolus versus 65279;UFH 60 IU/kg bolus, then titrated to ACT >200	Urgent or elective PCI	Parallel groups open
Droz d , 2001 n=50/50 follow-up: 24hrs, 30 days	65279;Enoxaparin 1 mg/kg bolus versus UFH 100 IU/kg bolus	PCI for stable angina	
Dudek , 2000 n=200/200 follow-up: 3 days	Enoxaparin 1 mg/kg bolus versus UFH titrated to ACT >300	PCI	
Dudek b (enox alone) , 2000 n=NA follow-up:	Enoxaparin 1 mg/kg bolus versus UFH titrated to ACT >300	PTCA complex lesionsCI	
Galeote , 2001 n=50/49 follow-up:	Enoxaparin 0.75 mg/kg bolus versus UFH 70 U/kg bolus, then titrated to ACT >200	PTCA patients with stable/unstable angina or AMI	
Rabah , 1999 n=30/30 follow-up:	Enoxaparin 1 mg/kg bolus versus 65279;UFH 10,000 IU bolus, then titrated to ACT >300	PCI for stable angina	Parallel groups open
STEEPLE , 2006 [NCT00077844] n=NA follow-up:	enoxaparin (0.5 or 0.75 mg per kilogram of body weight) versus unfractionated heparin (adjusted for activated clotting time)	elective percutaneous coronary intervention.	Parallel groups open
<b>enoxaparin+abciximab vs UFH</b>			
Dubek b (+abciximal) , 2001 n=NA	Enoxaparin 0.75 mg/kg bolus + abciximab versus UFH titrated to ACT >300	-	
<b>reviparin vs UFH</b>			

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Trial	Treatments	Patients	Trials design and methods
<b>REDUCE , 1996</b> n=306/306 follow-up: 3 days	65279;Reviparin 7,000 IU anti-Xa versus UFH 10,000 IU bolus	PTCA with stable/unstable angina	Parallel groups double blind Europe and Canada
<b>dalteparin vs UFH + anti Gp2b3a</b>			
<b>Natarajan (+ antiGp2b3a) , 2003</b> n=NA	Dalteparin 70 IU/kg bolus + GP IIb/IIIa inhibitorse/p versus 65279;UFH 70 IU/kg bolus +GPIIb/IIIa inhibitors	-	

## References

### Natarajan (without antiGp2b3a), 2003:

NatarajanMK, Turpie GA, Raco DL, Velianon JL,Mehta SR, Afzal A randomized comparison of dalteparin versus unfractionated heparin during percutaneous coronary interventions. J Am Coll Cardiol 2003;41(Suppl A):68A69A.xtPag

### ATOLL, 2010:

### Brieger, :

Brieger D, Collet JP, Silvain J, Landivier A, Barthlmy O, Beygui F, Bellemain-Appaix A, Mercadier A, Choussat R, Vignolles N, Costagliola D, Montalescot G Heparin or enoxaparin anticoagulation for primary percutaneous coronary intervention. Catheter Cardiovasc Interv 2011;77:182-90 [20578166] 10.1002/ccd.22674

### CRUISE, 2003:

Bhatt DL, Lee BI, Casterella PJ, Pulsipher M, Rogers M, Cohen M, Corrigan VE, Ryan TJ Jr, Breall JA, Moses JW, Eaton GM, Sklar MA, Lincoff AM Safety of concomitant therapy with eptifibatide and enoxaparin in patients undergoing percutaneous coronary intervention: results of the Coronary Revascularization Using Integrilin and Single bolus Enoxaparin Study. J Am Coll Cardiol 2003;41:20-5 [12570939]

### Drozd, 2001:

Drozd J, Opalinska E, Wojcik J, Madejczyk A.Pag The use of enoxaparin during percutaneous coronary angioplasty in patients with stable angina Kardiol Pol 2001;55:520524

### Dudek, 2000:

Dudek D, Dabrowski M, Ochala A, Lesaik M, Wnek A, Bryniarski Multicenter, prospective, double-blind randomized comparison of enoxaparin versus unfractionated heparin for percutaneous coronary interventions Am J Cardiol 2000;86(Suppl 8A):15i. imag

### Dudek b (enox alone), 2000:

Dudek D, Bartus S, Zymek P, Legutko J, Rzeszutko L, Janion M, Abciximab and enoxaparin administration during elective high-risk PTCA in patients with more than 3 days of ticlopidine pretreatment. J Am Coll Cardiol 2000;35(Suppl):91A

### Galeote, 2001:

Galeote G, Hussein M, Sobrino N, Calvo L, Yunda H, Sanchez- Combination abciximab and enoxaparin or unfractionated heparin during percutaneous coronary intervention: a randomised study Eur Heart J 2001;22(Suppl):663

### Rabah, 1999:

Rabah MM, Premmereur J, Graham M, Fareed J, Hoppensteadt DA, Grines LL, Grines CL Usefulness of intravenous enoxaparin for percutaneous coronary intervention in stable angina pectoris. Am J Cardiol 1999;84:1391-5 [10606110]

### STEEPLE, 2006:

Montalescot G, White HD, Gallo R, Cohen M, Steg PG, Aylward PE, Bode C, Chiariello M, King SB 3rd, Harrington RA, Desmet WJ, Macaya C, Steinhubl SR Enoxaparin versus unfractionated heparin in elective percutaneous coronary intervention. N Engl J Med 2006;355:1006-17 [16957147]

### Dubek b (+abciximal), 2001:

**REDUCE, 1996:**

Karsch KR, Preisack MB, Baidon R, Eschenfelder V, Foley D, Garcia EJ, Kaltenbach M, Meisner C, Selbmann HK, Serruys PW, Shiu MF, Sujatta M, Bonan R Low molecular weight heparin (reviparin) in percutaneous transluminal coronary angioplasty. Results of a randomized, double-blind, unfractionated heparin and placebo-controlled, multicenter trial (REDUCE trial). Reduction of Restenosis After PTCA, Early Administration of Reviparin in a Double-Blind Unfractionated Heparin and Placebo-Controlled Evaluation. J Am Coll Cardiol 1996;28:1437-43 [8917255]

**Natarajan (+ antiGp2b3a), 2003:**

## 4 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.

Rigorous meta-analysis method is used to populate TrialResults-center: widespread search of published and non published trials, study selection using pre-specified criteria, data extraction using standard form.

TrialResults-center is continually updated on a weekly basis. We continually search all new results (whatever their publication channel) and these news results are immediately added to the database with a maximum of 1 week.

TrialResults-center is non-profit and self-funded.