

# Clinical trials of A

TrialResults-center [www.trialresultscenter.org](http://www.trialresultscenter.org)

## 1 acute myocardial infarction

Trial	Treatments	Patients	Trials design and methods
<b>diltiazem vs</b>			
<a href="#">Machecourt , 1986</a> n=38/37 follow-up: 21 days	-	-	Parallel groups single blind
<b>Valsartan+ACE inhibitor vs ACE inhibitor only</b>			
<a href="#">VALIANT (valsartan+captopril) , 2003</a> n=4885/4909 follow-up: Median, 24.7 mo	Valsartan, 40 mg twice daily, plus captopril, 25 mg three times daily versus Captopril, 25 mg 3 times daily	patients within 10 days of a MI complicated by HF	Parallel groups Double blind 24
<b>paclitaxel eluting stent vs bare-metal stent</b>			
<a href="#">HAAMU-STENT , 2006</a> <i>unpublished</i> n=70/75 follow-up: 12 months	Taxus Express versus Bare-metal-stent	AMI - STEMI patients undergoing PCI	Parallel groups open Finland
<a href="#">HORIZONS-AMI Stent , 2008</a> n=2257/749 follow-up: 1 year	paclitaxel-eluting stents (Taxus) versus BMS (Express)	ST-elevation myocardial infarction	Factorial plan open
<a href="#">PASSION , 2006</a> [ISRCTN65027270] n=310/309 follow-up: 12 months (5y)	Taxus Express2 versus Express2 or Libert	Myocardial Infarction with ST-Segment Elevation	Parallel groups open The Netherlands
<b>Losartan vs Captopril</b>			
<a href="#">OPTIMAAL , 2002</a> n=2744/2733 follow-up: 2.7 y	Losartan, target dose of 50 mg daily versus Captopril, target dose of 50 mg 3 times daily	patients within 10 days of a confirmed acute myocardial infarction and heart failure during the acute phase or a new Q-wave anterior infarction or reinfarction	Parallel groups Double blind
<b>Valsartan vs Captopril</b>			

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>VALIANT (valsartan alone) , 2003</b> n=4909/4909 follow-up: Median, 24.7 mo	Valsartan, 160 mg twice daily versus Captopril, 50 mg 3 times daily	patients within 10 days of a MI complicated by HF	Parallel groups Double blind 24
<b>invasive strategy vs concervative strategy</b>			
<b>DANAMI , 1997</b> n=NA follow-up: 2.4y	invasive strategy of PTCA or CABG versus conservative strategy	patients who received thrombolytic treatment for a first acute myocardial infarction and with inducible myocardial ischemia (either symptomatic angina pectoris presenting spontaneously >36 hours after admission or during a predischarge exercise test or ST changes during exercise compatible with ischemia)	
<b>APSAC vs control</b>			
<b>APSIM , 1989</b> n=112/119 follow-up: 3 weeks	APSAC 30 U over 5 min versus control (conventional heparin therapy, 5,000 IU in a bolus injection)	patients with a first acute myocardial infarction within 5 h after the onset of symptoms	Parallel groups open France
<b>aspirin vs control</b>			
<b>Huddinge , 1988</b> n=10/10 follow-up: 30d (12m)	aspirin 500mg/d starting 12 h after admissionand and then intermittently every third day for one month versus no aspirin	patients with acute myocardial infarction	Parallel groups open
<b>Frankfurt , 1976</b> n=25/28 follow-up: 14d	-	-	Parallel groups
<b>autologous bone marrow stem cells vs control</b>			
<b>ASTAMi (Lunde) , 2006</b> n=50/50 follow-up: 6 months	intracoronary injection of autologous mononuclear BMC (stem cells $0.68 \cdot 10^8$ ) <i>versus</i> <i>control(Heparanizedplasma)</i>	patients with acute ST-elevation myocardial infarction of the anterior wall treated with percutaneous coronary intervention	parallel group open
<b>BOOS<sub>t</sub> (Meyer) , 2004</b> n=30/30 follow-up: 6 months	stem cells mean $2.46 \cdot 10^9$ <i>versus</i> <i>control(Heparanisedplasma)</i>	successful percutaneous coronary intervention (PCI) for acute ST-segment elevation myocardial infarction	parallel group open
<b>Chen , 2004</b> n=NA follow-up: 6 months	-	-	

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
Huang , 2006 n=20/20 follow-up: 6 months	intracoronary transplantation of autologous BM-MNC via a micro-catheter right after PCI (stem cells mean $1.8 \cdot 10^8$ ) <i>versus</i> <i>placebo(Heparanisedsaline)</i>	patients with first onset of acute inferior-wall myocardial infarction aged $\leq 75$ , treated with emergent percutaneous coronary intervention	parallel group open
Karpov , 2005 n=10/10 follow-up: 6 months	intracoronary injection of bone marrow mononuclear cells (stem cells mean $88.5 \cdot 10^6$ ) <i>versus</i> <i>control</i>	patients with acute myocardial infarction.	parallel group NA
Li , 2007 n=35/23 follow-up: 6 months	autologous peripheral blood stem cell transplantation by intracoronary infusion (stem cells mean $7.25 \cdot 10^7$ ) <i>versus</i> <i>control</i>	patients with AMI	parallel group open
MAGIC (cell infusion ) , 2004 n=10/7 follow-up:	intracoronary infusion of collected peripheral blood stem-cells <i>versus</i> <i>control</i>	patients with myocardial infarction who underwent coronary stenting for the culprit lesion of infarction	
MAGIC Cell-3-DES (Kang) , 2006 n=25/25 follow-up: 6 months	intracoronary infusion of mobilized peripheral blood stem cells by granulocyte colony-stimulating factor (stem cells $1-2 \cdot 10^9$ ) <i>versus</i> <i>control</i>	patients with myocardial infarction who underwent coronary revascularization with DES for the culprit lesion	parallel group open
Meluzin HD , 2006 n=22/22 follow-up: 3 months	intracoronar mononuclear bone marrow cells (stem cells $10^8$ ) <i>versus</i> <i>control(Cellsuspensionmedia)</i>	patients with a first acute myocardial infarction	parallel group open
Meluzin LD , 2006 n=22/22 follow-up: 3 months	intracoronar mononuclear bone marrow cells (stem cells $10^7$ ) <i>versus</i> <i>control(Cellsuspensionmedia)</i>	patients with a first acute myocardial infarction	parallel group open
Penicka , 2007 n=14/10 follow-up: 4 months	Intracoronary injection of autologous bone marrow-derived mononuclear cells (stem cells $26.4 \cdot 10^8$ ) <i>versus</i> <i>control</i>	patients with large anterior acute myocardial infarction	parallel group open

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
Ruan , 2005 n=9/11 follow-up: 6 months	intracoronary injection of bone-marrow cell (stem cells dose NA) versus control (Diluted serum)	with acute myocardial infarction and anterior descending coronary artery occlusion proven by angiography	parallel group open
Suarez de Lezo (cell) , 2007 n=10/10 follow-up: 3 months	intracoronary infusion of autologous mononuclear bone marrow cells ( $9 \times 10^8$ ) <i>versus</i> <i>control</i> (Salinecontaining0.1%heparin)	patients with revascularized anterior wall AMI and depressed left ventricular function (ejection fraction <45% )	parallel group open
TCT-STAMI (Ge) , 2006 n=10/10 follow-up: 6 months	emergent intracoronary autologous bone marrow cell transplantation ( $4 \times 10^7 SC$ ) <i>versus</i> <i>control</i>	patients admitted within 24 h after the onset of a first AMI	parallel group NA
<b>dazoxiben vs control</b>			
Jones , 1987 n=60/60 follow-up: 1m	-	-	Parallel groups
<b>early implantation of ICD after MI vs control</b>			
IRIS , 2009 [NCT00157768] n=445/453 follow-up: 37 months	prophylactic ICD implantation early after myocardial infarction versus optimal medical therapy alone	patients patients at increased risk 5 to 31 days after AMI	Parallel groups open
<b>hyperbaric oxygen vs control</b>			
Sharifi , 2004 n=NA follow-up:	-	after percutaneous coronary intervention for acute myocardial infarction or unstable angina pectoris	
Swift , 1992 n=NA follow-up:	-	patients within 1 week of acute myocardial infarction	
Thurston , 1973 n=NA follow-up:	-	acute myocardial infarction	
Hot MI , 1997 n=112 follow-up:	-	Patients with an acute myocardial infarction who received recombinant tissue plasminogen activator	
HOT MI pilot , 1997 n=66 follow-up:	-	Patients with an acute myocardial infarction (AMI) who received recombinant tissue plasminogen activator	
<b>IM lidocaine (without infusion) vs control</b>			

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>Koster and Dunning , 1985</b> n=2987/3037 follow-up: 1h for VT	lidocaine loading dose IM 400 mg versus no lidocaine	suspected acute myocardial infarction	Parallel groups Single-blind
<b>IV lidocaine infusion vs control</b>			
<b>Bennett , 1970</b> n=249/125 follow-up: 48h for VT	lidocaine loading dose IV 60mg, infusion 0.5-1.0 mg/min versus no lidocaine	suspected acute myocardial infarction	Parallel groups Open
<b>Pitt , 1971</b> n=108/114 follow-up: 48h for VT	lidocaine loading dose IV 75-100mg, infusion 2.5 mg/min versus no lidocaine	suspected acute myocardial infarction	Parallel groups Open
<b>Darby , 1972</b> n=103/100 follow-up: 48h for VT	lidocaine loading dose IM 200 mg, infusion 2.0 mg/min versus no lidocaine	suspected acute myocardial infarction	Parallel groups Open
<b>magnesium vs control</b>			
<b>ISIS-4 , 1995</b> n=29011/29030 follow-up:	24 h of intravenous magnesium sulphate (8 mmol initial bonus injection over about 15 minutes followed by 72 mmol in about 50 mLinfused over 24 h)4 versus no magnesium infusion	patients entering 1086 hospitals up to 24 h (median 8 h) after the onset of suspected acute myocardial infarction with no clear contraindications4	Parallel groups open
<b>Wu , 1992</b> n=125/102 follow-up:	2.5 g MgSO4 once or twice a day for 7-14 dayssce versus usual care	suspected AMI	Parallel groups double blind
<b>Zhu , 2002</b> n=1691/1488 follow-up:	100 mL (4 g) potassium-magnesium aspartate IV. for the first day, 50 ml for rest 4 datio versus routine AMI treatmentkB	AMI	Parallel groups open
<b>oxygen therapy vs control</b>			
<b>Rawles , 1976</b> n=NA follow-up:	oxygen administered by MC mask throughout the first 24 hours versus air	myocardial infarction	
<b>Ukholkina , 2005</b> n=NA follow-up:	-	patients with acute myocardial infarction	

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
Wilson , 1997 n=NA follow-up:	oxygen therapy versus control	patients presenting within 24 hours of onset of myocardial infarction	
<b>Propranolol vs control</b>			
Aronow , 1997 n=79/79 follow-up: 1 year	Propranolol 30 mg 3 times daily versus no propranolol	patients >=62 years of age with New York Heart Association functional class II or III CHF, prior Qwave myocardial infarction, and a LV ejection fraction <40% after 2 months of treatment with diuretics and ACE inhibitors	Parallel groups USA
<b>sulfinpyrazone vs control</b>			
Dutch sulphinpyrazone , 1986 n=50/50 follow-up: 21d	-	-	Parallel groups
<b>supersaturated oxygen vs control</b>			
AMIHOT II , 2000 [NCT00175058] n=222/79 follow-up:	90-minute intracoronary supersaturated oxygen (SSO(2)) infusion in the left anterior descending artery infarct territory versus control	patients with anterior ST-segment elevation myocardial infarction undergoing percutaneous coronary intervention within 6 hours of symptom onset	
AMIHOT , 2007 n=NA follow-up:	hyperoxemic reperfusion for 90 min using intracoronary aqueous oxygen versus normoxemic blood autoreperfusion	patients with acute anterior or large inferior AMI undergoing primary or rescue PCI (<24 h from symptom onset) and successful PCI	
<b>Tiapamil vs control</b>			
Eichler , 1985 n=16/16 follow-up:	Tiapamil 0.5-1 mg/kg plus 25mg/kg/min IV versus no treatment	-	Parallel groups double blind
<b>urokinase vs control</b>			
USIM , 1991 n=1128/1073 follow-up: in hospital	urokinase bolus dose of 1 million U repeated after 60 minutes plus heparin versus control (heparin alone)	patients with acute myocardial infarction within 4 hours of the onset of pain	Parallel groups open Italy
<b>verapamil vs control</b>			

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>Bussman , 1984</b> n=29/25 follow-up: 2 days	Verapamil 5 to 10 mg/h IV versus no treatment	-	Parallel groups open
<b>coumadin vs control (on top of aspirin)</b>			
<b>ASPECT-2</b> <b>(coumadin+ASA vs ASA) ,</b> <b>2002</b> n=298/289 follow-up: 1 year	coumadin(INR mean 2.4) +aspirin versus aspirin	Acute MI, unstable angina	Parallel groups open the Netherlands
<b>warfarin vs control (on top of aspirin)</b>			
<b>WARIS , 1999</b> n=1208/1206 follow-up: 65279;37 months	warfarin 2.84.8 versus placebo	survivors of acute myocardial infarction	Parallel groups double blind
<b>APRICOT-2 , 2002</b> n=135/139 follow-up: 3 months	moderate-intensity coumarin target INR 2-3 (+aspirin) versus aspirin	Acute MI after thrombolytics	Parallel groups open the Netherlands
<b>CARS (warafarin 3mg) ,</b> <b>1997</b> n=5410/3393 follow-up: 14 months	warfarin fixed dose 3mg/d + 80 mg ASA versus aspirin 160 mg/d	AMI	Parallel groups double blind North America
<b>CARS (warfarin 1mg) ,</b> <b>1997</b> n=2028/3393 follow-up: 14 months	warfarin 1mg/d + aspirin 80mg/d versus aspirin 160 mg/d	patients who had had myocardial infarction	Parallel groups double blind North America
<b>CHAMP , 2002</b> n=2522/2537 follow-up: 2.7 years	warfarin target INR 1.5-2.5 + aspirin 81 mg daily versus aspirin 162 mg/d	AMI (patients enrolled within 14 days of infarction)	Parallel groups open US
<b>LoWASA , 2004</b> n=1659/1641 follow-up: 5 years	warfarin fixed dose 1.25mg/d + ASA 75mg/d versus aspirin alone	AMI	Parallel groups open Sweden
<b>WARIS II (warfarin+ASA)</b> <b>, 2002</b> n=4927/4669 follow-up: 4 years	warfarin target INR 2-2.5 +ASA 75mg/d versus ASA 160mg/d	patients hospitalized for acute myocardial infarction	Parallel groups open Norway

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
Zibaenezhad , 2004 n=70/70 follow-up: 1 year	Warfarin target INR 65279;23 +aspirin versus aspirin 100 mg/day	Acute MI	Parallel groups open
<b>Angioguard vs conventional PCI</b>			
DIPLOMATE , 2004 n=32/28 follow-up: 1 month	Angioguard versus conventional PCI	patients with acute myocardial infarction	
Wang , 2003 n=20/20 follow-up: hospital stay	Angioguard versus conventional PCI	patients with acute myocardial infarction	open
<b>AngioJet vs conventional PCI</b>			
AiMI , 2006 n=240/240 follow-up: 1 month	AngioJet versus PCI alone	patients presenting within 12 h of symptom onset	open
Florence , 2004 n=50/50 follow-up: 1 month	AngioJet versus placebo	patients with a first acute myocardial infarction	
<b>AnjioJet vs conventional PCI</b>			
JETSTENT , 2010 n=256/245 follow-up: 6 months	AngioJet rheolytic thrombectomy versus direct stenting alone	patients with ST-elevation MI and at least moderate thrombus burden	Parallel groups open Italy
<b>GuardWire vs conventional PCI</b>			
ASPARAGUS , 2008 n=173/168 follow-up: hospital stay, 6 months	Guardwire versus conventional PCI	patients with acute myocardial infarction	open
EMERALD , 2005 n=252/249 follow-up: 1, 6 months	GuardWire versus angioplasty without distal protection	patients with ST-segment elevation myocardial infarction presenting within 6 hours of symptom onset and undergoing primary PCI or rescue intervention after failed thrombolysis	open
MICADO , 2007 n=80/74 follow-up: 1, 6 months	GuardWire versus PCI without distal protection	Patients with AMI within 24 hours from onset	open
Nanasato , 2004 n=34/30 follow-up: hospital stay	Guardwire versus conventional PCI	patients with acute myocardial infarction	open

continued...



<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
Ochala , 2007 n=57/63 follow-up: 6 months	GuardWire versus abciximab	patients with ST elevation acute myocardial infarction referred for primary percutaneous coronary intervention	open
Tahk , 2008 n=50/46 follow-up: 1, 6 months	GuardWire versus primary angioplasty without distal protection	AMI patients presenting within 12 h of onset of symptoms	open
<b>TVAC vs conventional PCI</b>			
VAMPIRE , 2004 n=180/175 follow-up: 8 months	TVAC versus conventional PCI	patients with acute myocardial infarction	
<b>primary angioplasty vs immediate thrombolysis</b>			
MAASTRICHT (Vermeer) , 1999 n=75/75 follow-up:	Transfer for primary PTCA versus immediate thrombolysis with tPA	patients with acute myocardial infarction initially admitted to a hospital without PTCA facilities	open
PRAGUE-1 , 2000 n=101/99 follow-up: 30 days	immediate transportation for primary angioplasty without pre-treatment with thrombolysis versus immediate thrombolysis with streptokinase	patients with acute myocardial infarction, presenting within 6 h of symptom onset at community hospitals without a catheterization laboratory	open
AIR-PAMI , 2002 n=71/66 follow-up:	Transfer for Primary Angioplasty versus immediate thrombolysis (various thrombolytic)	Patients with high-risk AMI (age >70 years, anterior MI, Killip class II/III, heart rate >100 beats/min or systolic BP <100 mm Hg), eligible for thrombolytic therapy	open
CAPTIM , 2002 n=421/419 follow-up:	Transfer for Primary Angioplasty versus prehospital fibrinolysis with accelerated alteplase	patients within 6 h of acute myocardial infarction with ST-segment elevation, initially managed by mobile emergency-care units	open
DANAMI-2 , 2003 n=567/562 follow-up: 30 days	Transfer for Primary Angioplasty versus immediate thrombolysis with tPA (accelared infusion)	patients with myocardial infarction with ST-segment elevation	Parallel groups open
PRAGUE-2 , 2003 n=429/421 follow-up: 30 days	immediate transport for primary percutaneous coronary intervention versus immediate thrombolysis with streptokinase	patients with acute ST elevation myocardial infarction presenting within <12 h to the nearest community hospital without a catheter laboratory	open

More details and results :

- antithrombotics for acute myocardial infarction in all type of patients at <http://www.trialresultscenter.org/go-Q36>
- beta-blockers for acute myocardial infarction in immediate beta-blockers at <http://www.trialresultscenter.org/go-Q41>
- beta-blockers for acute myocardial infarction in long term beta-blockers at <http://www.trialresultscenter.org/go-Q42>
- myocardial revascularization for acute myocardial infarction in facilitated PCI at <http://www.trialresultscenter.org/go-Q90>
- myocardial revascularization for acute myocardial infarction in all type of patients at <http://www.trialresultscenter.org/go-Q129>
- antiarrhythmic drugs for acute myocardial infarction in all type of patients at <http://www.trialresultscenter.org/go-Q130>
- Late revascularisation for acute myocardial infarction in late reperfusion at <http://www.trialresultscenter.org/go-Q134>
- myocardial revascularization for acute myocardial infarction in failed fibrinolysis (rescue revascularisation) at <http://www.trialresultscenter.org/go-Q135>
- calcium channel blockers for acute myocardial infarction in acute short term and post MI studies at <http://www.trialresultscenter.org/go-Q141>
- calcium channel blockers for acute myocardial infarction in acute (short term) treatment at <http://www.trialresultscenter.org/go-Q142>
- calcium channel blockers for acute myocardial infarction in long term studies at <http://www.trialresultscenter.org/go-Q143>
- nitrates for acute myocardial infarction in all type of patients at <http://www.trialresultscenter.org/go-Q144>
- angiotensin-Converting Enzyme Inhibitors for acute myocardial infarction in systematic early treatment (with or without sign of HF) at <http://www.trialresultscenter.org/go-Q145>
- angiotensin-Converting Enzyme Inhibitors for acute myocardial infarction in patients with or without HF at <http://www.trialresultscenter.org/go-Q146>
- angiotensin-Converting Enzyme Inhibitors for acute myocardial infarction in patients with left ventricular dysfunction after MI at <http://www.trialresultscenter.org/go-Q147>
- cholesterol lowering intervention for acute myocardial infarction in all type of patients at <http://www.trialresultscenter.org/go-Q162>
- anticoagulant for acute myocardial infarction in all type of patients at <http://www.trialresultscenter.org/go-Q172>
- PCI for acute myocardial infarction in all type of patients at <http://www.trialresultscenter.org/go-Q246>

- myocardial revascularization for acute myocardial infarction in patients in cardiogenic shock at <http://www.trialresultscenter.org/go-Q248>
- myocardial revascularization for acute myocardial infarction in  $\leq 6$ h from onset of symptoms at <http://www.trialresultscenter.org/go-Q249>

## References

### **Machecourt, 1986:**

### **VALIANT (valsartan+capropril), 2003:**

Pfeffer MA, McMurray JJ, Velazquez EJ, Rouleau JL, Kober L, Maggioni AP, Solomon SD, Swedberg K, Van de Werf F, White H, Leimberger JD, Henis M, Edwards S, Zelenkofske S, Sellers MA, Califf RM Valsartan, captopril, or both in myocardial infarction complicated by heart failure, left ventricular dysfunction, or both. *N Engl J Med* 2003 Nov 13;349:1893-906 [[14610160](#)]

### **HAAMU-STENT, 2006:**

unpublished

Tierala I, Syvaenne M, Kupari M Randomised comparison of apaclitaxel-eluting and a bare metal stent in STEMI-PCI. TheHAAMU-STENT-study Annual Scientific Meeting of the Transcatheter Cardiovascular Therapeutics; Washington, DC; Oct 22-27, 2006. Abstract 178.

### **HORIZONS-AMI Stent, 2008:**

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](#)

### **PASSION, 2006:**

Laarman GJ, Suttorp MJ, Dirksen MT, van Heerebeek L, Kiemeneij F, Slagboom T, van der Wieken LR, Tijssen JG, Rensing BJ, Patterson M Paclitaxel-eluting versus uncoated stents in primary percutaneous coronary intervention. *N Engl J Med* 2006;355:1105-13 [[16971717](#)]

Dirksen MT, Vink MA, Suttorp MJ, Tijssen JG, Patterson MS, Slagboom T, Kiemeneij F, Laarman GJ *EuroIntervention* 2008 May;4:64-70 [[19112781](#)]

### **OPTIMAAL, 2002:**

Dickstein K, Kjekshus J Effects of losartan and captopril on mortality and morbidity in high-risk patients after acute myocardial infarction: the OPTIMAAL randomised trial. *Optimal Trial in Myocardial Infarction with Angiotensin II Antagonist Losartan*. *Lancet* 2002 Sep 7;360:752-60 [[12241832](#)]

### **VALIANT (valsartan alone), 2003:**

Pfeffer MA, McMurray JJ, Velazquez EJ, Rouleau JL, Kober L, Maggioni AP, Solomon SD, Swedberg K, Van de Werf F, White H, Leimberger JD, Henis M, Edwards S, Zelenkofske S, Sellers MA, Califf RM Valsartan, captopril, or both in myocardial infarction complicated by heart failure, left ventricular dysfunction, or both. *N Engl J Med* 2003 Nov 13;349:1893-906 [[14610160](#)]

### **DANAMI, 1997:**

Madsen JK, Grande P, Saunamki K, Thayssen P, Kassis E, Eriksen U, Rasmussen K, Hauns S, Nielsen TT, Haghfelt T, Fritz-Hansen P, Hjelms E, Paulsen PK, Alstrup P, Arendrup H, Niebuhr-Jrgensen U, Andersen LI Danish multicenter randomized study of invasive versus conservative treatment in patients with inducible ischemia after thrombolysis in acute myocardial infarction (DANAMI). *DANish trial in Acute Myocardial Infarction*. *Circulation* 1997 Aug 5;96:748-55 [[9264478](#)]

Madsen JK, Nielsen TT, Grande P, Eriksen UH, Saunamki K, Thayssen P, Kassis E, Rasmussen K, Hauns S, Haghfelt T, Fritz-Hansen P, Hjelms E, Paulsen PK, Alstrup P, Arendrup H, Niebuhr-Jrgensen U, Andersen LI Revascularization compared to medical treatment in patients with silent vs. symptomatic residual ischemia after thrombolized myocardial infarction—the DANAMI study. *Cardiology* 2007;108:243-51 [[17114878](#)]

**APSIM, 1989:**

Bassand JP, Machecourt J, Cassagnes J, Anguenot T, Lussion R, Borel E, Peycelon P, Wolf E, Ducellier D Multicenter trial of intravenous anisoylated plasminogen streptokinase activator complex (APSAC) in acute myocardial infarction: effects on infarct size and left ventricular function. *J Am Coll Cardiol* 1989 Apr;13:988-97 [[2647817](#)]

**Huddinge, 1988:**

Rasmanis G, Vesterqvist O, Gren K, Edhag O, Henriksson P Effects of intermittent treatment with aspirin on thromboxane and prostacyclin formation in patients with acute myocardial infarction. *Lancet* 1988;2:245-7 [[2899236](#)]

**Frankfurt, 1976:**

Asasantin DVT nach Myokardinfarktp, imag Boehringer Ingelheim, 1976. (Boehringer Ingelheim internal report.)

**ASTAMi (Lunde), 2006:**

Lunde K, Solheim S, Aakhus S, Arnesen H, Abdelnoor M, Egeland T, Endresen K, Ilebekk A, Mangschau A, Fjeld JG, Smith HJ, Taraldsrud E, Grgaard HK, Bjrnheim R, Brekke M, Mller C, Hopp E, Ragnarsson A, Brinchmann JE, Forfang K Intracoronary injection of mononuclear bone marrow cells in acute myocardial infarction. *N Engl J Med* 2006;355:1199-209 [[16990383](#)] [10.1056/NEJMoa055706](#)

Beitnes JO, Hopp E, Lunde K, Solheim S, Arnesen H, Brinchmann JE, Forfang K, Aakhus S Long-term results after intracoronary injection of autologous mononuclear bone marrow cells in acute myocardial infarction: the ASTAMI randomised, controlled study. *Heart* 2009;95:1983-9 [[19833610](#)]

**BOOST (Meyer), 2004:**

Meyer GP, Wollert KC, Lotz J, Steffens J, Lippolt P, Fichtner S, Hecker H, Schaefer A, Arseniev L, Hertenstein B, Ganser A, Drexler H Intracoronary bone marrow cell transfer after myocardial infarction: eighteen months' follow-up data from the randomized, controlled BOOST (BOne marrOw transfer to enhance ST-elevation infarct regeneration) trial. *Circulation* 2006;113:1287-94 [[16520413](#)] [10.1161/CIRCULATIONAHA.105.575118](#)

Wollert KC, Meyer GP, Lotz J, Ringes-Lichtenberg S, Lippolt P, Breidenbach C, Fichtner S, Korte T, Hornig B, Messinger D, Arseniev L, Hertenstein B, Ganser A, Drexler H Intracoronary autologous bone-marrow cell transfer after myocardial infarction: the BOOST randomised controlled clinical trial. *Lancet* 2004;364:141-8 [[15246726](#)] [10.1016/S0140-6736\(04\)16626-9](#)

Meyer GP, Wollert KC, Lotz J, Pirr J, Rager U, Lippolt P, Hahn A, Fichtner S, Schaefer A, Arseniev L, Ganser A, Drexler H Intracoronary bone marrow cell transfer after myocardial infarction: 5-year follow-up from the randomized-controlled BOOST trial. *Eur Heart J* 2009;30:2978-84 [[19773226](#)]

**Chen, 2004:**

Chen SL, Fang WW, Ye F, Liu YH, Qian J, Shan SJ, Zhang JJ, Chunhua RZ, Liao LM, Lin S, Sun JP Effect on left ventricular function of intracoronary transplantation of autologous bone marrow mesenchymal stem cell in patients with acute myocardial infarction. *Am J Cardiol* 2004;94:92-5 [[15219514](#)]

**Huang, 2006:**

Huang RC, Yao K, Zou YZ, Ge L, Qian JY, Yang J, Yang S, Niu YH, Li YL, Zhang YQ, Zhang F, Xu SK, Zhang SH, Sun AJ, Ge JB [Long term follow-up on emergent intracoronary autologous bone marrow mononuclear cell transplantation for acute inferior-wall myocardial infarction] *Zhonghua Yi Xue Za Zhi* 2006;86:1107-10 [[16796836](#)]

**Karpov, 2005:**

Karpov RS, Popov SV, Markov VA, Suslova TE, Ryabov VV, Poponina YS, Krylov AL, Sazonova SV Autologous mononuclear bone marrow cells during reparative

regeneration after acute myocardial infarction. Bull Exp Biol Med 2005;140:640-3 [[16758644](#)]

**Li, 2007:**

Li ZQ, Zhang M, Jing YZ, Zhang WW, Liu Y, Cui LJ, Yuan L, Liu XZ, Yu X, Hu TS The clinical study of autologous peripheral blood stem cell transplantation by intracoronary infusion in patients with acute myocardial infarction (AMI). Int J Cardiol 2007;115:52-6 [[16822566](#)] [10.1016/j.ijcard.2006.04.005](#)

**MAGIC (cell infusion ), 2004:**

Kang HJ, Kim HS, Zhang SY, Park KW, Cho HJ, Koo BK, Kim YJ, Soo Lee D, Sohn DW, Han KS, Oh BH, Lee MM, Park YB Effects of intracoronary infusion of peripheral blood stem-cells mobilised with granulocyte-colony stimulating factor on left ventricular systolic function and restenosis after coronary stenting in myocardial infarction: the MAGIC cell randomised clinical trial. Lancet 2004;363:751-6 [[15016484](#)]

**MAGIC Cell-3-DES (Kang), 2006:**

Kang HJ, Lee HY, Na SH, Chang SA, Park KW, Kim HK, Kim SY, Chang HJ, Lee W, Kang WJ, Koo BK, Kim YJ, Lee DS, Sohn DW, Han KS, Oh BH, Park YB, Kim HS Differential effect of intracoronary infusion of mobilized peripheral blood stem cells by granulocyte colony-stimulating factor on left ventricular function and remodeling in patients with acute myocardial infarction versus old myocardial infarction: the MAGIC Cell-3-DES randomized, controlled trial. Circulation 2006;114:1145-51 [[16820564](#)] [10.1161/CIRCULATIONAHA.105.001107](#)

**Meluzin HD, 2006:**

Meluzin J, Mayer J, Groch L, Janousek S, Horncek I, Hlinomaz O, Kala P, Panovsk R, Prsek J, Kamnek M, Stancek J, Klabusay M, Korstek Z, Navrtil M, Dusek L, Vinklrkov J Autologous transplantation of mononuclear bone marrow cells in patients with acute myocardial infarction: the effect of the dose of transplanted cells on myocardial function. Am Heart J 2006;152:975.e9-15 [[17070173](#)] [10.1016/j.ahj.2006.08.004](#)

**Meluzin LD, 2006:**

Meluzin J, Mayer J, Groch L, Janousek S, Horncek I, Hlinomaz O, Kala P, Panovsk R, Prsek J, Kamnek M, Stancek J, Klabusay M, Korstek Z, Navrtil M, Dusek L, Vinklrkov J Autologous transplantation of mononuclear bone marrow cells in patients with acute myocardial infarction: the effect of the dose of transplanted cells on myocardial function. Am Heart J 2006;152:975.e9-15 [[17070173](#)] [10.1016/j.ahj.2006.08.004](#)

Meluzin J, Janousek S, Mayer J, Groch L, Horncek I, Hlinomaz O, Kala P, Panovsk R, Prsek J, Kamnek M, Stancek J, Klabusay M, Korstek Z, Navrtil M, Dusek L, Vinklrkov J Three-, 6-, and 12-month results of autologous transplantation of mononuclear bone marrow cells in patients with acute myocardial infarction. Int J Cardiol 2008;128:185-92 [[17764767](#)]

**Penicka, 2007:**

Penicka M, Horak J, Kobylka P, Pytlik R, Kozak T, Belohlavek O, Lang O, Skalicka H, Simek S, Palecek T, Linhart A, Aschermann M, Widimsky P Intracoronary injection of autologous bone marrow-derived mononuclear cells in patients with large anterior acute myocardial infarction: a prematurely terminated randomized study. J Am Coll Cardiol 2007;49:2373-4 [[17572255](#)] [10.1016/j.jacc.2007.04.009](#)

**Ruan, 2005:**

Ruan W, Pan CZ, Huang GQ, Li YL, Ge JB, Shu XH Assessment of left ventricular segmental function after autologous bone marrow stem cells transplantation in patients with acute myocardial infarction by tissue tracking and strain imaging. Chin Med J (Engl) 2005;118:1175-81 [[16117862](#)]

**Suarez de Lezo (cell), 2007:**

Suarez de Lezo J, Herrera C, Pan M, Romero M, Pavlovic D, Segura J, Sanchez J, Ojeda S, Torres A Rev Esp Cardiol 2007;60:357-65 [[17521544](#)]

**TCT-STAMI (Ge), 2006:**

Ge J, Li Y, Qian J, Shi J, Wang Q, Niu Y, Fan B, Liu X, Zhang S, Sun A, Zou Y Efficacy of emergent transcatheter transplantation of stem cells for treatment of acute myocardial infarction (TCT-STAMI). Heart 2006;92:1764-7 [[16775089](#)] [10.1136/hrt.2005.085431](#)

**Jones, 1987:**

Jones EW. A study of dazoxiben in the prevention of venous thrombosis after suspected myocardial infarction (MD Thesis).; Nottingham: Nottingham University, 1987:111-24

**IRIS, 2009:**

Steinbeck G, Andresen D, Seidl K, Brachmann J, Hoffmann E, Wojciechowski D, Kornacewicz-Jach Z, Sredniawa B, Lupkovic G, Hofgrtner F, Lubinski A, Rosenqvist M, Habets A, Wegscheider K, Senges J Defibrillator implantation early after myocardial infarction. *N Engl J Med* 2009;361:1427-36 [[19812399](#)]

**Sharifi, 2004:**

Sharifi M, Fares W, Abdel-Karim I, Koch JM, Sopko J, Adler D Usefulness of hyperbaric oxygen therapy to inhibit restenosis after percutaneous coronary intervention for acute myocardial infarction or unstable angina pectoris. *Am J Cardiol* 2004;93:1533-5 [[15194029](#)] [10.1016/j.amjcard.2004.03.009](#)

Sharifi M, Fares W, Abdel-Karim I, Petrea D, Koch JM, Adler D, Sopko J Inhibition of restenosis by hyperbaric oxygen: a novel indication for an old modality. *Cardiovasc Radiat Med* 2002;3:124-6 [[12974361](#)]

**Swift, 1992:**

Swift PC, Turner JH, Oxer HF, O'Shea JP, Lane GK, Woollard KV Myocardial hibernation identified by hyperbaric oxygen treatment and echocardiography in postinfarction patients: comparison with exercise thallium scintigraphy. *Am Heart J* 1992;124:1151-8 [[1442480](#)]

**Thurston, 1973:**

Thurston JG, Greenwood TW, Bending MR, Connor H, Curwen MP A controlled investigation into the effects of hyperbaric oxygen on mortality following acute myocardial infarction. *Q J Med* 1973;42:751-70 [[4606106](#)]

**Hot MI, 1997:**

Shandling AH, Ellestad MH, Hart GB, Crump R, Marlow D, Van Natta B, Messenger JC, Strauss M, Stavitsky Y Hyperbaric oxygen and thrombolysis in myocardial infarction: the "HOT MI" pilot study. *Am Heart J* 1997;134:544-50 [[9327714](#)]

Stavitsky Y, Shandling AH, Ellestad MH, Hart GB, Van Natta B, Messenger JC, Strauss M, Dekleva MN, Alexander JM, Mattice M, Clarke D Hyperbaric oxygen and thrombolysis in myocardial infarction: the 'HOT MI' randomized multicenter study. *Cardiology* 1998;90:131-6 [[9778551](#)]

Laden G. HOT MI pilot study. Hyperbaric oxygen and thrombolysis in myocardial infarction *American Heart Journal* 1998;136(4 Pt 1):749.

**HOT MI pilot, 1997:**

Shandling AH, Ellestad MH, Hart GB, Crump R, Marlow D, Van Natta B, Messenger JC, Strauss M, Stavitsky Y Hyperbaric oxygen and thrombolysis in myocardial infarction: the "HOT MI" pilot study. *Am Heart J* 1997;134:544-50 [[9327714](#)]

**Koster and Dunning, 1985:**

Koster RW, Dunning AJ Intramuscular lidocaine for prevention of lethal arrhythmias in the prehospitalization phase of acute myocardial infarction. *N Engl J Med* 1985;313:1105-10 [[3900727](#)]

**Bennett, 1970:**

Bennett MA, Wilner JM, Pentecost BL Controlled trial of lignocaine in prophylaxis of ventricular arrhythmias complicating myocardial infarction. *Lancet* 1970;2:909-11 [[4097285](#)]

**Pitt, 1971:**

Pitt A, Lipp H, Anderson ST Lignocaine given prophylactically to patients with acute myocardial infarction. *Lancet* 1971;1:612-6 [[4101228](#)]

**Darby, 1972:**

Darby S, Cruickshank JC, Bennett MA, Pentecost BL Trial of combined intramuscular and intravenous lignocaine in prophylaxis of ventricular tachyarrhythmias. *Lancet* 1972;1:817-9 [[4111579](#)]

**ISIS-4, 1995:**

ISIS-4: a randomised factorial trial assessing early oral captopril, oral mononitrate, and intravenous magnesium sulphate in 58,050 patients with suspected acute myocardial infarction. ISIS-4 (Fourth International Study of Infarct Survival) Collaborative Group. *Lancet* 1995;345:669-85 [[7661937](#)]

**Wu, 1992:**

**Zhu, 2002:**

**Rawles, 1976:**

Rawles JM, Kenmure AC Controlled trial of oxygen in uncomplicated myocardial infarction. *Br Med J* 1976;1:1121-3 [[773507](#)]

**Ukholkina, 2005:**

Ukholkina GB, Kostianov Iiu, Kuchkina NV, Grendo EP, Gofman IaB [Effect of oxygenotherapy used in combination with reperfusion in patients with acute myocardial infarction] *Kardiologija* 2005;45:59 [[16007057](#)]

**Wilson, 1997:**

Wilson AT, Channer KS Hypoxaemia and supplemental oxygen therapy in the first 24 hours after myocardial infarction: the role of pulse oximetry. *J R Coll Physicians Lond* 1997;31:657-61 [[9409501](#)]

**Aronow , 1997:**

Aronow WS, Ahn C, Kronzon I Effect of propranolol versus no propranolol on total mortality plus nonfatal myocardial infarction in older patients with prior myocardial infarction, congestive heart failure, and left ventricular ejection fraction  $\leq$  or = 40

**Dutch sulphinpyrazone, 1986:**

Funke Kpper AJ, Verheugt FWA, Jaarsma W, Roos JP.age/pj Funke Kpper AJ, Verheugt FWA, Jaarsma W, Roos JP. Failure of sulphinpyrazone to prevent left ventricular thrombosis in patients with AMI treated with oral anticoagulants Proceedings of X World Congress of Cardiology. Washington: 1986:419 (Abstract 2414)atio

**AMIHOT II , 2000:**

Haude M. AMIHOT-II: A prospective, randomized evaluation of supersaturated oxygen therapy after percutaneous coronary intervention in acute anterior myocardial infarction *Herz* 2007;32 (8):669

Stone GW, Martin JL, de Boer MJ, Margheri M, Bramucci E, Blankenship JC, Metzger DC, Gibbons RJ, Lindsay BS, Weiner BH, Lansky AJ, Krucoff MW, Fahy M, Boscardin WJ Effect of supersaturated oxygen delivery on infarct size after percutaneous coronary intervention in acute myocardial infarction. *Circ Cardiovasc Interv* 2009;2:366-75 [[20031745](#)] [10.1161/CIRCINTERVENTIONS.108.840066](#)

**AMIHOT, 2007:**

O'Neill WW, Martin JL, Dixon SR, Bartorelli AL, Trabattoni D, Oemrawsingh PV, Atsma DE, Chang M, Marquardt W, Oh JK, Krucoff MW, Gibbons RJ, Spears JR Acute Myocardial Infarction with Hyperoxemic Therapy (AMIHOT): a prospective, randomized trial of intracoronary hyperoxemic reperfusion after percutaneous coronary intervention. *J Am Coll Cardiol* 2007;50:397-405 [[17662390](#)] [10.1016/j.jacc.2007.01.099](#)

Stone GW, Martin JL, de Boer MJ, Margheri M, Bramucci E, Blankenship JC, Metzger DC, Gibbons RJ, Lindsay BS, Weiner BH, Lansky AJ, Krucoff MW, Fahy M, Boscardin WJ Effect of supersaturated oxygen delivery on infarct size after percutaneous coronary intervention in acute myocardial infarction. *Circ Cardiovasc Interv* 2009;2:366-75 [[20031745](#)] [10.1161/CIRCINTERVENTIONS.108.840066](#)

**Eichler, 1985:**

Eichler HG, Mabin TA, Commerford PJ, Lloyd EA, Beck W, Opie LH Tiapamil, a new calcium antagonist: hemodynamic effects in patients with acute myocardial infarction. *Circulation* 1985;71:779-86 [[3882269](#)]

**USIM, 1991:**

Rossi P, Bolognese L Comparison of intravenous urokinase plus heparin versus heparin alone in acute myocardial infarction. Urochinas per via Sistemica nell'Infarto Miocardico (USIM) Collaborative Group. *Am J Cardiol* 1991;68:585-92 [[1877476](#)]

**Bussman, 1984:**



Bussmann WD, Seher W, Gruengras M Reduction of creatine kinase and creatine kinase-MB indexes of infarct size by intravenous verapamil Am J Cardiol 1984;54:1224-30 [6391131]

**ASPECT-2 (coumadin+ASA vs ASA), 2002:**

van Es RF, Jonker JJ, Verheugt FW, Deckers JW, Grobbee DE Aspirin and coumadin after acute coronary syndromes (the ASPECT-2 study): a randomised controlled trial. Lancet 2002;360:109-13 [12126819]

**WARIS, 1999:**

Smith P, Arnesen H, Holme I The effect of warfarin on mortality and reinfarction after myocardial infarction. N Engl J Med 1990;323:147-52 [2194126]

**APRICOT-2, 2002:**

Brouwer MA, van den Bergh PJ, Aengevaeren WR, Veen G, Luijten HE, Hertzberger DP, van Boven AJ, Vromans RP, Uijen GJ, Verheugt FW Aspirin plus coumarin versus aspirin alone in the prevention of reocclusion after fibrinolysis for acute myocardial infarction: results of the Antithrombotics in the Prevention of Reocclusion In Coronary Thrombolysis (APRICOT)-2 Trial. Circulation 2002;106:659-65 [12163424]

**CARS (warafarin 3mg), 1997:**

Randomised double-blind trial of fixed low-dose warfarin with aspirin after myocardial infarction. Coumadin Aspirin Reinfarction Study (CARS) Investigators. Lancet 1997;350:389-96 [9259652]

**CARS (warfarin 1mg), 1997:**

Randomised double-blind trial of fixed low-dose warfarin with aspirin after myocardial infarction. Coumadin Aspirin Reinfarction Study (CARS) Investigators. Lancet 1997;350:389-96 [9259652]

**CHAMP, 2002:**

Fiore LD, Ezekowitz MD, Brophy MT, Lu D, Sacco J, Peduzzi P Department of Veterans Affairs Cooperative Studies Program Clinical Trial comparing combined warfarin and aspirin with aspirin alone in survivors of acute myocardial infarction: primary results of the CHAMP study. Circulation 2002;105:557-63 [11827919]

**LoWASA, 2004:**

Herlitz J, Holm J, Peterson M, Karlson BW, Haglid Evander M, Erhardt L Effect of fixed low-dose warfarin added to aspirin in the long term after acute myocardial infarction; the LoWASA Study. Eur Heart J 2004;25:232-9 [14972424]

**WARIS II (warfarin+ASA), 2002:**

Hurlen M, Abdelnoor M, Smith P, Erikssen J, Arnesen H Warfarin, aspirin, or both after myocardial infarction. N Engl J Med 2002;347:969-74 [12324552]

**Zibaeenezhad, 2004:**

Zibaeenezhad MJ, Mowla A, Sorbi MH Warfarin and aspirin versus aspirin alone in patients with acute myocardial infarction: a pilot study. Angiology 2004;55:17-20 [14759085]

**DIPLOMATE, 2004:**

Lefevre T, Guyon P, Reimers B, Fauvel JM, Pansieri M, Dewez MP Eur Heart J 2004;25(Suppl.):420m

**Wang, 2003:**

Wang L, Nguyen T, Yang X, Yang C.8L imag Am J Cardiol 2003;92(Suppl. 6A):38L

**AiMI, 2006:**

Ali A, Cox D, Dib N, Brodie B, Berman D, Gupta N, Browne K, Iwaoka R, Azrin M, Stapleton D, Setum C, Popma J J Am Coll Cardiol 2006;48:244-52 [16843170]  
10.1016/j.jacc.2006.03.044

**Florence, 2004:**

Antoniucci D, Valenti R, Migliorini A, Parodi G, Memisha G, Santoro GM, Sciagr R Am J Cardiol 2004;93:1033-5 [15081450] 10.1016/j.amjcard.2004.01.011

**JETSTENT, 2010:**

Migliorini A, Stabile A, Rodriguez AE, Gandolfo C, Rodriguez Granillo AM, Valenti R, Parodi G, Neumann FJ, Colombo A, Antoniucci D Comparison of AngioJet Rheolytic Thrombectomy Before Direct Infarct Artery Stenting With Direct Stenting Alone in Patients With Acute Myocardial Infarction The JETSTENT Trial. J Am Coll Cardiol 2010 Oct 12;56:1298-306 [20691553] 10.1016/j.jacc.2010.06.011

**ASPARAGUS, 2008:**

Muramatsu T http://www.tctmd.com/ Show.aspx?id=58944

**EMERALD, 2005:**



Stone GW, Webb J, Cox DA, Brodie BR, Qureshi M, Kalynych A, Turco M, Schultheiss HP, Dulas D, Rutherford BD, Antoniucci D, Krucoff MW, Gibbons RJ, Jones D, Lansky AJ, Mehran R JAMA 2005;293:1063-72 [15741528] 10.1001/jama.293.9.1063

**MICADO, 2007:**

Matsuo A, Inoue N, Suzuki K, Nakamura R, Fujita H, Miki S, Yokoi Y J Invasive Cardiol 2007;19:132-8 [17341781]

**Nanasato, 2004:**

Nanasato M, Hirayama H, Muramatsu T, Unno K, Shimano M, Matsushita K, J Am Coll Cardiol 2004;43(Suppl. 1):246A

**Ochala, 2007:**

Ochala A, Smolka G, Wojakowski W, Gabrylewicz B, Garbocz P, Tendera M Kardiol Pol 2007;65:672-80; discussion 681-3 [17629829]

**Tahk, 2008:**

Tahk SJ, Choi BJ, Choi SY, Yoon MH, Gwon HC, Hong GR, Kim YJ, Hur SH, Kim KB, Koo BK, Lee SH, Yoon J Int J Cardiol 2008;123:162-8 [17490759] 10.1016/j.ijcard.2007.03.124

Tahk S-J, Chae IH, Choi S-Y, et al. imag Circulation 2004;110 [Suppl., abstr]mag

**VAMPIRE, 2004:**

Isshiki T. (1 July 2008) http:// www.tctmd.com/Show.aspx?id=56032

**MAASTRICHT (Vermeer), 1999:**

Vermeer F, Oude Ophuis AJ, vd Berg EJ, Brunninkhuis LG, Werter CJ, Boehmer AG, Lousberg AH, Dassen WR, Br FW Prospective randomised comparison between thrombolysis, rescue PTCA, and primary PTCA in patients with extensive myocardial infarction admitted to a hospital without PTCA facilities: a safety and feasibility study. Heart 1999;82:426-31 [10490554]

**PRAGUE-1, 2000:**

Widimsk P, Groch L, Zelzko M, Aschermann M, Bednr F, Suryapranata H Multicentre randomized trial comparing transport to primary angioplasty vs immediate thrombolysis vs combined strategy for patients with acute myocardial infarction presenting to a community hospital without a catheterization laboratory. The PRAGUE study. Eur Heart J 2000;21:823-31 [10781354]

**AIR-PAMI, 2002:**

Grines CL, Westerhausen DR Jr, Grines LL, Hanlon JT, Logemann TL, Niemela M, Weaver WD, Graham M, Boura J, O'Neill WW, Balestrini C A randomized trial of transfer for primary angioplasty versus on-site thrombolysis in patients with high-risk myocardial infarction: the Air Primary Angioplasty in Myocardial Infarction study. J Am Coll Cardiol 2002;39:1713-9 [12039480]

**CAPTIM, 2002:**

Bonnefoy E, Lapostolle F, Leizorovicz A, Steg G, McFadden EP, Dubien PY, Cattan S, Boullenger E, Machecourt J, Lacroute JM, Cassagnes J, Dissait F, Touboul P Primary angioplasty versus prehospital fibrinolysis in acute myocardial infarction: a randomised study. Lancet 2002;360:825-9 [12243916]

**DANAMI-2, 2003:**

Fosbl EL, Thune JJ, Kelbaek H, Andersen HR, Saunamki K, Nielsen TT, Mortensen LS, Kber L Long-term outcome of primary angioplasty compared with fibrinolysis across age groups: a Danish Multicenter Randomized Study on Fibrinolytic Therapy Versus Acute Coronary Angioplasty in Acute Myocardial Infarction (DANAMI-2) substudy. Am Heart J 2008 Aug;156:391-6 [18657676]

Madsen JK, Grande P, Saunamki K, Thayssen P, Kassis E, Eriksen U, Rasmussen K, Hauns S, Nielsen TT, Haghfelt T, Fritz-Hansen P, Hjelms E, Paulsen PK, Alstrup P, Arendrup H, Niebuhr-Jrgensen U, Andersen LI Danish multicenter randomized study of invasive versus conservative treatment in patients with inducible ischemia after thrombolysis in acute myocardial infarction (DANAMI). DANish trial in Acute Myocardial Infarction. Circulation 1997 Aug 5;96:748-55 [9264478]

Madsen JK, Nielsen TT, Grande P, Eriksen UH, Saunamki K, Thayssen P, Kassis E, Rasmussen K, Hauns S, Haghfelt T, Fritz-Hansen P, Hjelms E, Paulsen PK, Alstrup P, Arendrup H, Niebuhr-Jrgensen U, Andersen LI Revascularization compared to medical treatment in patients with silent vs. symptomatic residual ischemia after thrombolysed myocardial infarction—the DANAMI study. Cardiology 2007;108:243-51 [17114878]

Andersen HR, Nielsen TT, Rasmussen K, Thuesen L, Kelbaek H, Thayssen P, Abildgaard U, Pedersen F, Madsen JK, Grande P, Villadsen AB, Krusell LR, Haghfelt T, Lomholt P, Husted SE, Vigholt E, Kjaergard HK, Mortensen LS A comparison of coronary angioplasty with fibrinolytic therapy in acute myocardial infarction. N Engl J Med 2003 Aug 21;349:733-42 [12930925]

**PRAGUE-2, 2003:**

Widimsk P, Budesnsk T, Vorc D, Groch L, Zelzko M, Aschermann M, Branny M, St'sek J, Formnek P Long distance transport for primary angioplasty vs immediate thrombolysis in acute myocardial infarction. Final results of the randomized national multicentre trial—PRAGUE-2. Eur Heart J 2003;24:94-104 [12559941]

## 2 post stroke

Trial	Treatments	Patients	Trials design and methods
<b>rivaroxaban vs aspirin</b>			
<a href="#">NAVIGATE ESUS , 2018</a> [NCT02313909] n=3609/3604	rivaroxaban (at a daily dose of 15 mg) versus aspirin (at a daily dose of 100 mg)	patients with recent ischemic stroke that was presumed to be from cerebral embolism but without arterial stenosis, lacune, or an identified cardioembolic source	
<b>warfarin vs aspirin</b>			
<a href="#">SWAT , 1998</a> n=NA follow-up: 2 years	warfarin (INR 2.0 to 3.0) versus Enteric-coated aspirin 650 mg 12-hourly	-	Parallel groups open USA
<b>anticoagulant vs no anticoagulant</b>			
<a href="#">Baker , 1964</a> n=NA follow-up:	unnamed anticoagulant (TQ (2 to 2.5 times control in seconds), started in hospital versus no treatment	-	Parallel groups open
<a href="#">Bradshaw , 1975</a> n=NA follow-up:	warfarin or phenindione for 18 mo; TP time 2x control versus no treatment	-	Parallel groups open UK
<a href="#">LHSPS , 1999</a> n=NA follow-up: 2 years	unfractionated heparin 12.500 IU/d plus usual therapy versus usual therapy	-	Parallel groups open Italy
<a href="#">VA Study , 1961</a> n=NA follow-up: 11 months	coumadin or dicumarol, prothrombin activity 20% of normal versus no treatment	-	Parallel groups open USA
<a href="#">Wallace , 1964</a> n=NA follow-up: 9.75 months	phenindione or warfarin, Quick test 20% to 35% of normal (50% after 10 months) versus no treatment	-	Parallel groups open Australia
<b>anticoagulant vs placebo</b>			
<a href="#">McDevitt , 1959</a> n=NA follow-up: 34 months	dicumarol or warfarin, Quisk test 2 to 2.5 times control in seconds versus placebo	-	Parallel groups single-blind USA
<b>aspirin vs placebo</b>			

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
Canadian study (CCSG) , 1978 n=144/139 follow-up: ND	aspirin 325 mg/d versus placebo	-	Factorial plan Double blind
Swedish study , 1987 n=253/252 follow-up: 2 y	aspirin 1,500 mg/d versus placebo	-	
UK-TIA low dose , 1988 n=806/814 follow-up: 4 y	aspirin 300 mg/d versus placebo	-	
UK-TIA high dose , 1988 n=815/814 follow-up: 2y	aspirin 1,200 mg/d versus placebo	-	
SALT , 1991 n=676/684 follow-up: 32 mo	aspirin 75 mg/d versus placebo	-	
Reuther , 1976 n=30/30 follow-up: 2 y	aspirin 1,500 mg/d versus placebo	-	
AITA , 1975 n=162/157 follow-up: 1 y	aspirin 1,300 mg/d versus placebo	-	
DCS , 1980 n=101/102 follow-up: 25 mo	aspirin 1,000 mg/d versus placebo	-	
AICLA , 1981 n=198/204 follow-up: 3 y	aspirin 990 mg/d versus placebo	-	
Lindblad , 1991 n=117/115 follow-up: 6 mo	aspirin 75 mg/d, during 6 months versus placebo	-	
Danish low-dose , 1986 n=150/151 follow-up: 23 mo	aspirin 50-100 mg/d (mean 54 mg/d) versus placebo	-	
ESPS 2 , 1996 n=1649/1649 follow-up: 2 y	aspirin 50 mg/d versus placebo	-	
<b>atorvastatin vs placebo</b>			

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>SPARCL , 2006</b> [NCT00147602] n=2365/2366 follow-up: 4.9y (median)	atorvastatin 80mg daily versus placebo	patients who had had a stroke or TIA within one to six months before study entry, had low-density lipoprotein (LDL) cholesterol levels of 2.6 to 4.9 mmol per liter, and had no known coronary heart disease	Parallel groups double blind
<b>dicoumarol vs placebo</b>			
<b>Howard , 1963</b> n=NA follow-up: 1 year	dicoumarol, TP 15 to 25% of normal versus placebo	-	Parallel groups single-blind USA
<b>Nat-Coop , 1962</b> n=NA follow-up: 13 months	heparin 50 mg 4-hourly iv then dicoumarol, Quick test 15% to 25% of control versus placebo	-	Parallel groups single-blind USA
<b>folic acid, vit B12 and vit B6 vs placebo</b>			
<b>VITATOPS , 2010</b> [NCT00097669X]  Parallel groups double-blind 20 countries	]n=4089/4075 follow-up: 3.4 y	folic acid and vitamins B12 and B6 in a single tablet versus placebo	patients with recent stroke or TIA (within the past seven months)
<b>simvastatin vs placebo</b>			
<b>HPS (post stroke sub group) , 2004</b> n=920/900 follow-up:	simvastatin 40mg daily versus placebo	adults with cerebrovascular disease, total cholesterol $\geq$ 35 mmol/L and without coronaro disease (n=1820)	Parallel groups double blind
<b>telmisartan vs placebo</b>			
<b>PROFESS , 2008</b> n=NA follow-up:	telmisartan 80 mg/d versus placebo	-	
<b>high dose - folic acid, vit B12 and vit B6 vs low dose - folic acid, vit B12 and vit B6</b>			
<b>VISP (Toole) , 2004</b> n=1827/1853 follow-up: 2 y	high-dose of folic acid, pyridoxine (vitamin B6), and cobalamin (vitamin B12) versus low-dose of folic acid, pyridoxine (vitamin B6), and cobalamin (vitamin B12)	adults with nondisabling cerebral infarction	Parallel groups double blind United States, Canada, Scotland
<b>Starflex vs medical treatment</b>			

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>CLOSURE I , 2010</b> <i>unpublished</i> [NCT00201461] n=447/462 follow-up: 2 years	patent foramen ovale closure using the Starflex device versus best medical therapy: aspirin (325 mg daily) and/or warfarin (target INR = 2.5)	patients with a stroke and/or transient ischemic attack due to presumed paradoxical embolism through a patent foramen ovale	Parallel groups open US, Canada

More details and results :

- cholesterol lowering intervention for post stroke in all type of patients at <http://www.trialresultscenter.org/go-Q153>
- anti hypertensive agents for post stroke in all type of patients at <http://www.trialresultscenter.org/go-Q410>
- antiplatelets drug for post stroke in all type of patients at <http://www.trialresultscenter.org/go-Q411>
- anticoagulant for post stroke in all type of patients at <http://www.trialresultscenter.org/go-Q413>
- prevention for post stroke in patients with prior stroke or TIA at <http://www.trialresultscenter.org/go-Q421>
- foramen ovale closure for post stroke in all type of patients at <http://www.trialresultscenter.org/go-Q430>

## References

### NAVIGATE ESUS, 2018:

Hart RG, Sharma M, Mundl H, Kasner SE, Bangdiwala SI, Berkowitz SD, Swaminathan B, Lavados P, Wang Y, Wang Y, Davalos A, Shamalov N, Mikulik R, Cunha L, Lindgren A, Arauz A, Lang W, Czlonkowska A, Eckstein J, Gagliardi RJ, Amarenco P, Ameriso SF, Tatlisum Rivaroxaban for Stroke Prevention after Embolic Stroke of Undetermined Source. *N Engl J Med* 2018;378:2191-2201 [29766772]

### SWAT, 1998:

Stewart B, Shuaib F, Veloso F. Stroke Prevention with Warfarin or Aspirin Trial (SWAT) *Stroke* 1998;29:304.

### Baker, 1964:

Baker RN, Schwartz WS, Rose MD Transient ischemic strokes. A report of a study of anticoagulant therapy. *Neurology* 1966;16:841-7.

Baker RN, Schwartz WS, Rose MD Transient ischemic strokes. A report of a study of anticoagulant therapy. *Neurology* 1966;16:841-7.

Baker RN, Schwartz WS, Rose MD Transient ischemic strokes. A report of a study of anticoagulant therapy. *Neurology* 1966;16:841-7.

### Bradshaw, 1975:

Bradshaw P, Brennan S Trial of long-term anticoagulant therapy in the treatment of small stroke associated with a normal carotid angiogram. *Journal of Neurology, Neurosurgery and Psychiatry* 1975;38:642-7.

Bradshaw P, Brennan S Trial of long-term anticoagulant therapy in the treatment of small stroke associated with a normal carotid angiogram. *Journal of Neurology, Neurosurgery and Psychiatry* 1975;38:642-7.

Bradshaw P, Brennan S Trial of long-term anticoagulant therapy in the treatment of small stroke associated with a normal carotid angiogram. *Journal of Neurology, Neurosurgery and Psychiatry* 1975;38:642-7.

### LHSPS, 1999:

Fortini A, Bonechi G, Carnovali M, Olivo G, Rinaldi G, Gensini GF Multi-centric study on ischemic cerebral re-infarct prevention with low-dose heparin: the informatic system [Sistema informatico dello studio clinico controllato multicentrico sulla prevenzione del reinfarto cerebrale ischemico con eparina a basso dosaggio]. *Rivista di Neurobiologica*

Fortini A, Bonechi G, Carnovali M, Olivo G, Rinaldi G, Gensini GF Multi-centric study on ischemic cerebral re-infarct prevention with low-dose heparin: the informatic system [Sistema informatico dello studio clinico controllato multicentrico sulla prevenzione del reinfarto cerebrale ischemico con eparina a basso dosaggio]. *Rivista di Neurobiologica*

Fortini A, Bonechi G, Carnovali M, Olivo G, Rinaldi G, Gensini GF Multi-centric study on ischemic cerebral re-infarct prevention with low-dose heparin: the informatic system [Sistema informatico dello studio clinico controllato multicentrico sulla prevenzione del reinfarto cerebrale ischemico con eparina a basso dosaggio]. *Rivista di Neurobiologica*

**VA Study, 1961:**

Baker RN. An evaluation of anticoagulant therapy in the treatment of cerebrovascular disease. Report of the Veterans Administration Cooperative Study of Atherosclerosis, Neurology Section Neurology 1961;11:1328.

**Wallace, 1964:**

WALLACE DC CEREBRAL VASCULAR DISEASE IN RELATION TO LONG-TERM ANTICOAGULANT THERAPY. J Chronic Dis 1964;17:527-37 [[14168625](#)]

**McDevitt, 1959:**

McDEVITT E, GROCH SN, WRIGHT IS A cooperative study of cerebrovascular disease; methodology and a preliminary report on the use of anticoagulants. Circulation 1959;20:215-23 [[13671708](#)]

McDowell F, McDevitt E, Wright IS. Anticoagulant therapy: five years experience with the patient with an established cerebrovascular accident.-ms Archives of Neurology 1963;8:20914

**Canadian study (CCSG), 1978:**

A randomized trial of aspirin and sulfinpyrazone in threatened stroke. The Canadian Cooperative Study Group. N Engl J Med 1978;299:53-9 [[351394](#)] [10.1056/NEJM197807132990201](#)

**Swedish study , 1987:**

High-dose acetylsalicylic acid after cerebral infarction. A Swedish Cooperative Study. Stroke 1987;18:325-34 [[2882626](#)]

**UK-TIA low dose , 1988:**

Farrell B, Godwin J, Richards S, Warlow C The United Kingdom transient ischaemic attack (UK-TIA) aspirin trial: final results. J Neurol Neurosurg Psychiatry 1991;54:1044-54 [[1783914](#)]

**UK-TIA high dose , 1988:**

Farrell B, Godwin J, Richards S, Warlow C The United Kingdom transient ischaemic attack (UK-TIA) aspirin trial: final results. J Neurol Neurosurg Psychiatry 1991;54:1044-54 [[1783914](#)]

**SALT , 1991:**

Swedish Aspirin Low-Dose Trial (SALT) of 75 mg aspirin as secondary prophylaxis after cerebrovascular ischaemic events. The SALT Collaborative Group. Lancet 1991;338:1345-9 [[1682734](#)]

**Reuther , 1976:**

Stuttgart Schattauer 1978;97-106 [[0](#)]

**AITA, 1975:**

Fields WS, Lemak NA, Frankowski RF, Hardy RJ Controlled trial of aspirin in cerebral ischemia. Part II: surgical group. Stroke 1978;9:309-19 [[354098](#)]

**DCS, 1980:**

Sorensen PS, Pedersen H, Marquardsen J, Petersson H, Heltberg A, Simonsen N, Munck O, Andersen LA Acetylsalicylic acid in the prevention of stroke in patients with reversible cerebral ischemic attacks. A Danish cooperative study. Stroke 1983;14:15-22 [[6337425](#)]

**AICLA, 1981:**

Bousser MG, Eschwege E, Haguenu M, Lefaucconnier JM, Thibult N, Touboul D, Touboul PJ "AICLA" controlled trial of aspirin and dipyridamole in the secondary prevention of athero-thrombotic cerebral ischemia. Stroke 1983;14:5-14 [[6401878](#)]

**Lindblad , 1991:**

Lindblad B, Persson NH, Takolander R, Bergqvist D Does low-dose acetylsalicylic acid prevent stroke after carotid surgery? A double-blind, placebo-controlled randomized trial. Stroke 1993;24:1125-8 [[8342184](#)]

**Danish low-dose, 1986:**

Barnett HJ, Eliasziw M, Meldrum HE Drugs and surgery in the prevention of ischemic stroke. N Engl J Med 1995;332:238-48 [[7808491](#)] [10.1056/NEJM199501263320408](#)

**ESPS 2 , 1996:**

Diener HC, Cunha L, Forbes C, Sivenius J, Smets P, Lowenthal A European Stroke Prevention Study. 2. Dipyridamole and acetylsalicylic acid in the secondary prevention of stroke. J Neurol Sci 1996;143:1-13 [[8981292](#)]

**SPARCL, 2006:**

Amarenco P, Bogousslavsky J, Callahan A 3rd, Goldstein LB, Hennerici M, Rudolph AE, Sillensen H, Simunovic L, Szarek M, Welch KM, Zivin JA High-dose atorvastatin after stroke or transient ischemic attack. N Engl J Med 2006 Aug 10;355:549-59 [[16899775](#)]

Amarenco P, Benavente O, Goldstein LB, Callahan A 3rd, Silleesen H, Hennerici MG, Gilbert S, Rudolph AE, Simunovic L, Zivin JA, Welch KM Results of the Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) trial by stroke subtypes. Stroke 2009;40:1405-9 [[19228842](#)]

**Howard, 1963:**

HOWARD FA, COHEN P, HICKLER RB, LOCKES, NEWCOMB T, TYLER HR Survival following stroke JAMA 1963;183:921-5 [[13955115](#)]

**Nat-Coop, 1962:**

FISHER CM Anticoagulant therapy in cerebral thrombosis and cerebral embolism. A national cooperative study, interim report. Neurology 1961;11(4)Pt 2:119-31 [[13699939](#)]

**VITATOPS, 2010:**

Hankey GJ. The Vitamins to Prevent Stroke (VITATOPS) trial: Results of a double-blind, placebo-controlled, randomised trial of B-vitamin therapy in 8164 patients with recent transient ischaemic attack or stroke. 2010 European Stroke Conference: May 26, 2010; Barcelona, Spain

B vitamins in patients with recent transient ischaemic attack or stroke in the VITAMINS TO Prevent Stroke (VITATOPS) trial: a randomised, double-blind, parallel, placebo-controlled trial. Lancet Neurol 2010 Aug 3: [[20688574](#)] [10.1016/S1474-4422\(10\)70187-3](#)

**HPS (post stroke sub group), 2004:**

Collins R, Armitage J, Parish S, Sleight P, Peto R Effects of cholesterol-lowering with simvastatin on stroke and other major vascular events in 20536 people with cerebrovascular disease or other high-risk conditions. Lancet 2004;363:757-67 [[15016485](#)]

**PROFESS, 2008:**

**VISP (Toole), 2004:**

Spence JD, Bang H, Chambless LE, Stampfer MJ Vitamin Intervention For Stroke Prevention trial: an efficacy analysis. Stroke 2005 Nov;36:2404-9 [[16239629](#)]

Toole JF, Malinow MR, Chambless LE, Spence JD, Pettigrew LC, Howard VJ, Sides EG, Wang CH, Stampfer M Lowering homocysteine in patients with ischemic stroke to prevent recurrent stroke, myocardial infarction, and death: the Vitamin Intervention for Stroke Prevention (VISP) randomized controlled trial. JAMA 2004 Feb 4;291:565-75 [[14762035](#)]

**CLOSURE I, 2010:**

unpublished

Furlan AJ, Reisman M, Massaro J, Mauri L, Adams H, Albers GW, Felberg R, Herrmann H, Kar S, Landzberg M, Raizner A, Wechsler L Study design of the CLOSURE I Trial: a prospective, multicenter, randomized, controlled trial to evaluate the safety and efficacy of the STARFlex septal closure system versus best medical therapy in patients with stroke or transient ischemic attack due to presumed paradoxical embolism through a patent foramen ovale. Stroke 2010;41:2872-83 [[21051670](#)] [10.1161/STROKEAHA.110.593376](#)

Furlan AJ, Reisman M, Massaro J, Mauri L, Adams H, Albers GW, Felberg R, Herrmann H, Kar S, Landzberg M, Raizner A, Wechsler L Closure or medical therapy for cryptogenic stroke with patent foramen ovale. N Engl J Med 2012 Mar 15;366:991-9 [[22417252](#)] [10.1056/NEJMoa1009639](#)

### 3 post myocardial infarction

Trial	Treatments	Patients	Trials design and methods
<b>class I drugs vs control</b>			
<b>BASIS , 1990</b> n=100/114 follow-up: 1 year	individualized antiarrhythmic treatment versus no antiarrhythmic therapy	patients with persisting asymptomatic complex arrhythmias after myocardial infarction	Parallel groups open
<b>early amiodarone vs control</b>			
<b>BASIS , 1990</b> n=98/14 follow-up: 65279;12 mo	amiodarone 1 g for 5 d; then 200 mg/d started within 4 weeks of AMI versus no amiodarone (usual care)	patients with persisting asymptomatic complex arrhythmias after myocardial infarction (Lown class 3 or 4b in >2 of 24 h)	Parallel groups open

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>Navarro-Lopez , 1993</b> n=115/123 follow-up: 24 mo	amiodarone 600 mg/d for 1 week, 400 mg/d for 1 week then 200 mg/d started 10-30 d after AMI versus no amiodarone	patients who have had MI with a left ventricular ejection fraction of 20 to 45% and >or = 3 ventricular premature complexes per hour (pairs or runs) - 3 VPOs/h, pairs or runs of VT	Parallel groups open Spain
<b>omega-3 Fatty acids vs control</b>			
<b>OMEGA , 2009</b> [NCT00251134] n=1940/1911 follow-up: 1 year	omega-3 fatty acids 1g daily (and standard medical therapy) versus standard medical therapy alone	Patients within 3-14 days after a non-ST-elevation myocardial infarction (NSTEMI) or ST-elevation myocardial infarction (STEMI)	Parallel groups open Germany
<b>coumadin vs control (on top of aspirin)</b>			
<b>ASPECT-2 (coumadin+ASA vs ASA) , 2002</b> n=298/289 follow-up: 1 year	coumadin(INR mean 2.4) +aspirin versus aspirin	Acute MI, unstable angina	Parallel groups open the Netherlands
<b>warfarin vs control (on top of aspirin)</b>			
<b>WARIS , 1999</b> n=1208/1206 follow-up: 65279;37 months	warfarin 2.84.8 versus placebo	survivors of acute myocardial infarction	Parallel groups double blind
<b>APRICOT-2 , 2002</b> n=135/139 follow-up: 3 months	moderate-intensity coumarin target INR 2-3 (+aspirin) versus aspirin	Acute MI after thrombolytics	Parallel groups open the Netherlands
<b>CARS (warafarin 3mg) , 1997</b> n=5410/3393 follow-up: 14 months	warfarin fixed dose 3mg/d + 80 mg ASA versus aspirin 160 mg/d	AMI	Parallel groups double blind North America
<b>CARS (warfarin 1mg) , 1997</b> n=2028/3393 follow-up: 14 months	warfarin 1mg/d + aspirin 80mg/d versus aspirin 160 mg/d	patients who had had myocardial infarction	Parallel groups double blind North America
<b>CHAMP , 2002</b> n=2522/2537 follow-up: 2.7 years	warfarin target INR 1.5-2.5 + aspirin 81 mg daily versus aspirin 162 mg/d	AMI (patients enrolled within 14 days of infarction)	Parallel groups open US
<b>LoWASA , 2004</b> n=1659/1641 follow-up: 5 years	warfarin fixed dose 1.25mg/d + ASA 75mg/d versus aspirin alone	AMI	Parallel groups open Sweden

continued...



<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>WARIS II (warfarin+ASA) , 2002</b> n=4927/4669 follow-up: 4 years	warfarin target INR 2-2.5 +ASA 75mg/d versus ASA 160mg/d	patients hospitalized for acute myocardial infarction	Parallel groups open Norway
<b>Zibaenezhad , 2004</b> n=70/70 follow-up: 1 year	Warfarin target INR 65279;23 +aspirin versus aspirin 100 mg/day	Acute MI	Parallel groups open
<b>any anticoagulant vs placebo</b>			
<b>Sixty Plus reinfarction Study , 1980</b> n=NA follow-up: 2 years	anticoagulant versus placebo	over 60 years of age	Parallel groups double blind
<b>aspirin vs placebo</b>			
<b>CDPA , 1976</b> n=758/771 follow-up: 1.83 y	Aspirin (324 mg) 3x/d versus Placebo	MI survivors	Parallel groups Double blind USA
<b>Cardiff I , 1974</b> n=615/624 follow-up: 2 years	Aspirin (300 mg) 1x/d versus Placebo	MI survivors	Parallel groups Double blind UK
<b>Cardiff II , 1979</b> n=832/850 follow-up: 1 y	Aspirin (300 mg) 3x/d for one year versus Placebo	patients with myocardial infarction	Parallel groups Double blind South Wales
<b>Vogel , 1979</b> n=672/668 follow-up: 1.75 y (mean)	Aspirin (1.5 g daily) on an average period of 22 months versus Placebo	-	Parallel groups Double blind Germany
<b>AMIS , 1980</b> [NCT00000491] n=2267/2257 follow-up: >3 y	Aspirin (500 mg) 2x/d for at least 3 years versus Placebo	men and women who had had a documented myocardial infarction	Parallel groups Double blind USA
<b>GAMIS , 1980</b> n=317/309 follow-up: 2 y	Aspirin (500 mg) 3x/d for 2 years versus Placebo	patients who had survived a myocardial infarction for 30-42 days	Parallel groups Double blind Germany, Austria,
<b>PARIS , 1980</b> n=810/406 follow-up: 41 mo	Aspirin (324 mg) 3x/d versus Placebo	patients who had recovered from myocardial infarction	Parallel groups Double blind USA, UK

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>JAMIS , 1999</b> n=250/230 follow-up: 1.3 y (mean)	Aspirin (81 mg) 1x/d versus No antiplatelets	patients with AMI within 1 month from the onset of symptoms	Parallel groups Open Japan
<b>azimilide vs placebo</b>			
<b>ALIVE , 2004</b> n=NA follow-up: 1y	azimilide 100 mg versus placebo	post-MI patients with depressed LVF	Parallel groups double blind
<b>bezafibrate vs placebo</b>			
<b>BECAIT , 1996</b> n=47/45 follow-up: 5.0 years	bezafibrate 200 mg three times daily versus placebo	dyslipidaemic male survivors of myocardial infarction who were younger than 45 years at the time of the event	Parallel groups double blind Sweden
<b>BIP , 2000</b> n=1548/1542 follow-up: 6.2 y	bezafibrate 400 mg/d versus placebo	patients with a previous myocardial infarction or stable angina, total cholesterol of 180 to 250 mg/dL, HDL-C <or =45 mg/dL, triglycerides <or =300 mg/dL, and low-density lipoprotein cholesterol <or =180 mg/dL	Parallel groups double blind Israel
<b>canakinumab vs placebo</b>			
<b>CANTOS , 2017</b> [NCT01327846] n=10066 follow-up: 36 months	Quarterly Subcutaneous Canakinumab 50mg, 150mg, 300mg for 36 months versus placebo	Stable Post-myocardial Infarction Patients With Elevated hsCRP	double-blind
<b>clofibrate+niacin vs placebo</b>			
<b>Carlson (Stockholm) , 1977</b> n=279/276 follow-up: 5 years	clofibrate, 1 g twice daily, and nicotinic acid 1 g three times daily versus control	survivors of a myocardial infarction below 70 years of age	Parallel groups open Sweden
<b>coumadin vs placebo</b>			
<b>ASPECT , 1994</b> n=1700/1704 follow-up: 37 months (range 6-76)	nicoumalone or phenprocoumon, target INR 2.84.8 versus placebo	hospital survivors of myocardial infarction	Parallel groups double blind
<b>d,l sotalol vs placebo</b>			
<b>Julian , 1982</b> n=1456 follow-up: 1 year	sotalol 320 mg once daily versus placebo	surviving an acute myocardial infarction	Parallel groups double blind
<b>dabigatran vs placebo</b>			

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>REDEEM , 2009</b> <i>unpublished</i> [NCT00621855] n=1501/373 follow-up: 6 months	dabigatran 4 dosages (50mg twice daily, 75mg twice daily, 110mg twice daily, 150mg twice daily) versus placebo	patients with recent acute coronary syndromes (ST- or non-ST-elevation myocardial infarction)	Parallel groups double blind
<b>diltiazem vs placebo</b>			
<b>MDPIT , 1988</b> n=1234/1232 follow-up: 25 months (at least 12 months)	Diltiazem 60mgx4 versus placebo	Patient aged 25 to 75 years, admitted to coronary care units with a documented acute myocardial infarction	Parallel groups Double blind US, Canada
<b>dipyridamol + aspirin vs placebo</b>			
<b>PARIS , 1980</b> n=810/406 follow-up: 41 months (mean)	Aspirin (324 mg) + dipyridamole (75 mg) 3x/d versus Placebo	patients who had recovered from myocardial infarction	Parallel groups Double blind USA and UK
<b>PARIS-II , 1986</b> n=1563/1565 follow-up: 23.4 months	Aspirin (330 mg) + dipyridamole (75 mg) 3x/d versus Placebo	patients who had recovered from myocardial infarction, suffered from 4 weeks to 4 months previously	Parallel groups Double blind USA and UK
<b>early amiodarone vs placebo</b>			
<b>CAMIAT , 1991</b> n=NA follow-up: 24 mo	amiodarone 10 mg/kg per d for 3 weeks then 300-400 mg/d started 6-45 d after AMI versus placebo	patients with acute myocardial infarction within the previous 6-30 days and >10 VPDs/h for 18 h or a run of VT	Parallel groups double blind
<b>Ceremuzyński , 1992</b> n=305/308 follow-up: 12 mo	amiodarone 800 mg/d for 1 week then 200-400 mg/d started 5-7 d after AMI versus placebo	No need for antiarrhythmic therapy	Parallel groups double blind
<b>Hockings , 1987</b> n=59/70 follow-up: 642 mo	amiodarone 200 mg 3 times daily for 1 wk; then 200 mg/d started <8-10 d after AMI versus placebo	patients with AMI - Absence of VF or VT >3 beats	Parallel groups double blind
<b>pravastatin vs placebo</b>			
<b>CARE , 1996</b> n=2081/2078 follow-up: 5 years	pravastatin 40 mg/d versus placebo	men and women with myocardial infarction who had plasma totalcholesterol levels below 240 mg per deciliter (mean,209) and low-density lipoprotein (LDL) cholesterollevels of 115 to 174 mg per deciliter	Parallel groups double blind USA, Canada

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>LIPID , 1998</b> n=4512/4502 follow-up: 6.1 years	pravastatin 40 mg/d versus placebo	patients with previous myocardial infarction or unstable angina and a baseline plasma cholesterol concentration of 4.0-7.0 mmol/L	Parallel groups double blind Australie et Nouvelle Zlande
<b>PACT , 2004</b> n=1710/1689 follow-up: 30 days	pravastatin initiated within 24 hours of onset of symptoms and for 4 weeks versus placebo	patients with unstable angina, non-ST-segment elevation myocardial infarction, or ST-segment elevation myocardial infarction <24 hours	Parallel groups double blind
<b>simvastatin vs placebo</b>			
<b>4S , 1994</b> n=2221/2223 follow-up: 5.4 years	simvastatin 20 or 40 mg/d, target CT between 3 et 5.2 mmol/l versus placebo	patients with angina pectoris or previous myocardial infarction and serum cholesterol 5.5-8.0 mmol/L on a lipid-lowering diet	Parallel groups double blind Scandinavia
<b>verapamil vs placebo</b>			
<b>DAVIT I , 1984</b> n=1751/1747 follow-up: 6 months	verapamil 120mgx3 versus placebo	-	Parallel groups Double blind Danish
<b>DAVIT II , 1990</b> n=878/897 follow-up: 16 months	verapamil 120mgx3 for 18 months versus placebo	patients <76years with diagnosis of acute MI	Parallel groups Double blind Danish
<b>CRIS , 1996</b> n=531/542 follow-up: 23.5 months	verapamil retard 360 mg daily versus placebo	patients admitted for acute myocardial infarction	Parallel groups Double blind Italy
<b>Danish study , 1984</b> n=1729/1718 follow-up: 12 months	verapamil 0.1mg/kg IV plus 3x120mg orally versus placebo	patients under 75 years of age admitted to the CCU with a suspicion of acute myocardial infarction	Parallel groups double blind Danish
<b>ticagrelor vs placebo (on top aspirin)</b>			
<b>PEGASUS 60mg , 2015</b> [NCT01225562] n=7045/7067 follow-up: 2.75 y (median)	ticagrelor at a dose of 60 mg twice daily versus placebo	patients who had had a myocardial infarction 1 to 3 years earlier	Parallel groups double-blind
<b>PEGASUS 90mg , 2015</b> [NCT01225562] n=7050/7067 follow-up: 2.75 y (median)	-	patients who had had a myocardial infarction 1 to 3 years earlier	double-blind
<b>vorapaxar vs placebo (on top aspirin)</b>			

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>TRA-2P TIMI 50 , 2012</b> [NCT00526474] n=13225/13244 follow-up: 2.5 y (median)	vorapaxar (SCH 530348) 2.5-mg daily versus placebo (added to the existing standard of care for preventing heart attack and stroke (eg, aspirin, clopidogrel)	patients with a known history of atherosclerosis (MI, ischemic stroke, or peripheral vascular disease)	Parallel groups double-blind
<b>warfarin vs placebo (on top of aspirin)</b>			
<b>Williams , 1997</b> n=6/5 follow-up: 2.5 months	warfarin target INR 65279;22.5 +aspirin versus placebo +aspirin	Acute MI, unstable angina	Parallel groups double blind
<b>any anticoagulant vs aspirin</b>			
<b>EPSIM , 1982</b> n=652/651 follow-up: 29 months (range 6-59)	anticoagulant versus aspirin 500mg three times daily	patients surviving myocardial infarction	Parallel groups open
<b>coumadin vs aspirin</b>			
<b>ASPECT-2 (coumadin alone) , 2002</b> n=325/336 follow-up: 1 year (range 0-26 months)	coumadin (phenprocoumon or acenocoumarol) target INR 3-4 versus aspirin 80mg daily	Acute MI, unstable angina	Parallel groups open the Netherlands
<b>dipyridamol + aspirin vs aspirin</b>			
<b>PARIS , 1980</b> n=810/810 follow-up: 41 months	Aspirin (324 mg) + dipyridamole (75 mg) 3x/d versus Aspirin (324 mg) 3x/d	patuents who had recovered from myocardial infarction	Parallel groups Double blind USA and GB
<b>warfarin vs aspirin</b>			
<b>WARIS II (warfarin alone) , 2002</b> n=1216/1206 follow-up: 48 months	warfarin target INR 2.8-4.2 versus ASA 160mg/d	patients hospitalized for acute myocardial infarction	Parallel groups NA Norway
<b>atorvastatin high dose vs atorvastatin</b>			
<b>TNT , 2005</b> [NCT00327691] n=4995/5006 follow-up: 4.9 years	80 mg of atorvastatin daily versus 10 mg of atorvastatin daily	Chronic coronary artery disease LDL cholesterol <3.4 mmol/L	Parallel groups double blind 14 countries
<b>atorvastatin high dose vs lovastatin</b>			
<b>Vascular basis , 2005</b> n=197/103 follow-up: 1 year	atorvastatin (80 mg) with or without vitamin C and E versus low dose lovastatin (5 mg)	Chronic coronary artery disease	Parallel groups double blind
<b>low fat diet vs mediterranean-style diet</b>			

continued...

Trial	Treatments	Patients	Trials design and methods
Tuttle , 2008 n=NA follow-up: 24 months	low-fat versus Mediterranean-style diets	First MI survivors	Parallel groups open

More details and results :

- cholesterol lowering intervention for post myocardial infarction in all type of patients at <http://www.trialresultscenter.org/go-Q45>
- anticoagulant for post myocardial infarction in all type of patients at <http://www.trialresultscenter.org/go-Q173>
- antiarrhythmic drugs for post myocardial infarction in all type of patients at <http://www.trialresultscenter.org/go-Q251>
- calcium channel blockers for post myocardial infarction in all type of patients at <http://www.trialresultscenter.org/go-Q252>
- antiplatelets drug for post myocardial infarction in all type of patient at <http://www.trialresultscenter.org/go-Q277>
- omega-3 fatty acids for post myocardial infarction in all type of patients at <http://www.trialresultscenter.org/go-Q283>
- antithrombotics for post myocardial infarction in all type of patients at <http://www.trialresultscenter.org/go-Q364>
- secondary prevention for post myocardial infarction in all type of patients at <http://www.trialresultscenter.org/go-Q449>
- anti inflammatory drugs for post myocardial infarction in all type of patients at <http://www.trialresultscenter.org/go-Q684>

## References

### **BASIS, 1990:**

Burkart F, Pfisterer M, Kiowski W, Follath F, Burckhardt D Effect of antiarrhythmic therapy on mortality in survivors of myocardial infarction with asymptomatic complex ventricular arrhythmias: Basel Antiarrhythmic Study of Infarct Survival (BASIS) J Am Coll Cardiol 1990 Dec;16:1711-8 [2254558]

### **BASIS, 1990:**

Burkart F, Pfisterer M, Kiowski W, Follath F, Burckhardt D Effect of antiarrhythmic therapy on mortality in survivors of myocardial infarction with asymptomatic complex ventricular arrhythmias: Basel Antiarrhythmic Study of Infarct Survival (BASIS) J Am Coll Cardiol 1990;16:1711-8 [2254558]

### **Navarro-Lopez, 1993:**

Navarro-Lpez F, Cosin J, Marrugat J, Guindo J, Bayes de Luna A Comparison of the effects of amiodarone versus metoprolol on the frequency of ventricular arrhythmias and on mortality after acute myocardial infarction. SSSD Investigators. Spanish Study on Sudden Death. Am J Cardiol 1993;72:1243-8 [7504880]

### **OMEGA, 2009:**

Senges Randomized Trial of Omega-3 Fatty Acids on Top of Modern Therapy After Acute Myocardial Infarction: The OMEGA Trial ACC.09/i2, Orlando, FL, March 2009 [0]

Rauch B, Schiele R, Schneider S, Diller F, Victor N, Gohlke H, Gottwik M, Steinbeck G, Del Castillo U, Sack R, Worth H, Katus H, Spitzer W, Sabin G, Senges J OMEGA, a randomized, placebo-controlled trial to test the effect of highly purified omega-3 fatty acids on top of modern guideline-adjusted therapy after myocardial infarction. Circulation 2010;122:2152-9 [21060071] 10.1161/CIRCULATIONAHA.110.948562

### **ASPECT-2 (coumadin+ASA vs ASA), 2002:**

van Es RF, Jonker JJ, Verheugt FW, Deckers JW, Grobbee DE Aspirin and coumadin after acute coronary syndromes (the ASPECT-2 study): a randomised controlled trial. Lancet 2002;360:109-13 [12126819]

### **WARIS, 1999:**

Smith P, Arnesen H, Holme I The effect of warfarin on mortality and reinfarction after myocardial infarction. N Engl J Med 1990;323:147-52 [2194126]

### **APRICOT-2, 2002:**

Brouwer MA, van den Bergh PJ, Aengevaeren WR, Veen G, Luijten HE, Hertzberger DP, van Boven AJ, Vromans RP, Uijen GJ, Verheugt FW Aspirin plus coumarin versus aspirin alone in the prevention of reocclusion after fibrinolysis for acute myocardial infarction: results of the Antithrombotics in the Prevention of Reocclusion In Coronary Thrombolysis (APRICOT)-2 Trial. Circulation 2002;106:659-65 [12163424]

**CARS (warafirin 3mg), 1997:**

Randomised double-blind trial of fixed low-dose warfarin with aspirin after myocardial infarction. Coumadin Aspirin Reinfarction Study (CARS) Investigators. *Lancet* 1997;350:389-96 [[9259652](#)]

**CARS (warfarin 1mg), 1997:**

Randomised double-blind trial of fixed low-dose warfarin with aspirin after myocardial infarction. Coumadin Aspirin Reinfarction Study (CARS) Investigators. *Lancet* 1997;350:389-96 [[9259652](#)]

**CHAMP, 2002:**

Fiore LD, Ezekowitz MD, Brophy MT, Lu D, Sacco J, Peduzzi P Department of Veterans Affairs Cooperative Studies Program Clinical Trial comparing combined warfarin and aspirin with aspirin alone in survivors of acute myocardial infarction: primary results of the CHAMP study. *Circulation* 2002;105:557-63 [[11827919](#)]

**LoWASA, 2004:**

Herlitz J, Holm J, Peterson M, Karlson BW, Haglid Evander M, Erhardt L Effect of fixed low-dose warfarin added to aspirin in the long term after acute myocardial infarction; the LoWASA Study. *Eur Heart J* 2004;25:232-9 [[14972424](#)]

**WARIS II (warfarin+ASA), 2002:**

Hurlen M, Abdelnoor M, Smith P, Erikssen J, Arnesen H Warfarin, aspirin, or both after myocardial infarction. *N Engl J Med* 2002;347:969-74 [[12324552](#)]

**Zibaeenezhad, 2004:**

Zibaeenezhad MJ, Mowla A, Sorbi MH Warfarin and aspirin versus aspirin alone in patients with acute myocardial infarction: a pilot study. *Angiology* 2004;55:17-20 [[14759085](#)]

**Sixty Plus reinfarction Study, 1980:**

A double-blind trial to assess long-term oral anticoagulant therapy in elderly patients after myocardial infarction. Report of the Sixty Plus Reinfarction Study Research Group. *Lancet* 1980;2:989-94 [[6107674](#)]

**CDPA, 1976:**

, Aspirin in coronary heart disease. The Coronary Drug Project Research Group. *J Chronic Dis* 1976; 29:625-42 [[789390](#)]

**Cardiff I, 1974:**

Elwood P, Trial of acetylsalicylic acid in the secondary prevention of mortality from myocardial infarction. *Br Med J (Clin Res Ed)* 1981; 282:481 [[6780093](#)]

**Cardiff II, 1979:**

Elwood PC, Sweetnam PM, Aspirin and secondary mortality after myocardial infarction. *Lancet* 1979; 2:1313-5 [[92668](#)]

**Vogel, 1979:**

*Folia Haematol* 1979; 106:797-803 [[0](#)]

**AMIS, 1980:**

, The aspirin myocardial infarction study: final results. The Aspirin Myocardial Infarction Study research group. *Circulation* 1980; 62:V79-84 [[7438383](#)]

, A randomized, controlled trial of aspirin in persons recovered from myocardial infarction. *JAMA* 1980; 243:661-9 [[6985998](#)]

**GAMIS, 1980:**

Breiddin K, Loew D, Lechner K, Oberla K, Walter E, The German-Austrian aspirin trial: a comparison of acetylsalicylic acid, placebo and phenprocoumon in secondary prevention of myocardial infarction. On behalf of the German-Austrian Study Group. *Circulation* 1980; 62:V63-72 [[6777073](#)]

**PARIS, 1980:**

, Persantine and aspirin in coronary heart disease. The Persantine-Aspirin Reinfarction Study Research Group. *Circulation* 1980; 62:449-61 [[7398002](#)]

**JAMIS, 1999:**

Yasue H, Ogawa H, Tanaka H, Miyazaki S, Hattori R, Saito M, Ishikawa K, Masuda Y, Yamaguchi T, Motomiya T, Tamura Y, Effects of aspirin and trapidil on cardiovascular events after acute myocardial infarction. Japanese Antiplatelets Myocardial Infarction Study (JAMIS) Investigators. *Am J Cardiol* 1999; 83:1308-13 [[10235086](#)]

**ALIVE, 2004:**

Pratt CM, Singh SN, Al-Khalidi HR, Brum JM, Holroyde MJ, Marcello SR, Schwartz PJ, Camm AJ The efficacy of azimilide in the treatment of atrial fibrillation in the presence of left ventricular systolic dysfunction: results from the Azimilide Postinfarct Survival Evaluation (ALIVE) trial. *J Am Coll Cardiol* 2004 Apr 7;43:1211-6 [[15063432](#)]

Camm AJ, Pratt CM, Schwartz PJ, Al-Khalidi HR, Spyt MJ, Holroyde MJ, Karam R, Sonnenblick EH, Brum JM Mortality in patients after a recent myocardial infarction: a randomized, placebo-controlled trial of azimilide using heart rate variability for risk stratification. *Circulation* 2004 Mar 2;109:990-6 [[14967728](#)]

Camm AJ, Karam R, Pratt CM The azimilide post-infarct survival evaluation (ALIVE) trial. *Am J Cardiol* 1998 Mar 19;81:35D-39D [[9537221](#)]

#### **BECAIT, 1996:**

Ruotolo G, Ericsson CG, Tettamanti C, Karpe F, Grip L, Svane B, Nilsson J, de Faire U, Hamsten A Treatment effects on serum lipoprotein lipids, apolipoproteins and low density lipoprotein particle size and relationships of lipoprotein variables to progression of coronary artery disease in the Bezafibrate Coronary Atherosclerosis Intervention Trial (BECAIT). *J Am Coll Cardiol* 1998;32:1648-56 [[9822092](#)]

Ericsson CG Results of the Bezafibrate Coronary Atherosclerosis Intervention Trial (BECAIT) and an update on trials now in progress. *Eur Heart J* 1998;19 Suppl H:H37-41 [[9717064](#)]

Ericsson CG, Hamsten A, Nilsson J, Grip L, Svane B, de Faire U Angiographic assessment of effects of bezafibrate on progression of coronary artery disease in young male postinfarction patients. *Lancet* 1996;347:849-53 [[8622389](#)]

de Faire U, Ericsson CG, Hamsten A, Nilsson J Design features of a five-year Bezafibrate Coronary Atherosclerosis Intervention Trial (BECAIT). *Drugs Exp Clin Res* 1995;21:105-24 [[7555614](#)]

#### **BIP, 2000:**

, Secondary prevention by raising HDL cholesterol and reducing triglycerides in patients with coronary artery disease: the Bezafibrate Infarction Prevention (BIP) study. *Circulation* 2000; 102:21-7 [[10880410](#)]

Goldenberg I, Boyko V, Tennenbaum A, Tanne D, Behar S, Guetta V Long-term benefit of high-density lipoprotein cholesterol-raising therapy with bezafibrate: 16-year mortality follow-up of the bezafibrate infarction prevention trial. *Arch Intern Med* 2009;169:508-14 [[19273782](#)]

#### **CANTOS, 2017:**

Ridker PM, Thuren T, Zalewski A, Libby P Interleukin-1? inhibition and the prevention of recurrent cardiovascular events: rationale and design of the Canakinumab Anti-inflammatory Thrombosis Outcomes Study (CANTOS). *Am Heart J* 2011;162:597-605 [[21982649](#)]

#### **Carlson (Stockholm), 1977:**

Carlson LA, Danielson M, Ekberg I, Klintemar B, Rosenhamer G, Reduction of myocardial reinfarction by the combined treatment with clofibrate and nicotinic acid. *Atherosclerosis* 1977; 28:81-6 [[911371](#)]

Carlson LA, Rosenhamer G, Reduction of mortality in the Stockholm Ischaemic Heart Disease Secondary Prevention Study by combined treatment with clofibrate and nicotinic acid. *Acta Med Scand* 1988; 223:405-18 [[3287837](#)]

#### **ASPECT, 1994:**

Effect of long-term oral anticoagulant treatment on mortality and cardiovascular morbidity after myocardial infarction. Anticoagulants in the Secondary Prevention of Events in Coronary Thrombosis (ASPECT) Research Group. *Lancet* 1994;343:499-503 [[7906757](#)]

#### **Julian, 1982:**

Julian DG, Camm AJ, Frangin G, Janse MJ, Munoz A, Schwartz PJ, Simon P Randomised trial of effect of amiodarone on mortality in patients with left-ventricular dysfunction after recent myocardial infarction: EMIAT. *European Myocardial Infarct Amiodarone Trial Investigators. Lancet* 1997 Mar 8;349:667-74 [[9078197](#)]

Julian DG, Prescott RJ, Jackson FS, Szekely P Controlled trial of sotalol for one year after myocardial infarction. *Lancet* 1982 May 22;1:1142-7 [[6122937](#)]

#### **REDEEM, 2009:**

unpublished

Oldgren J, Budaj A, Granger CB, Khder Y, Roberts J, Siegbahn A, Tijssen JG, Van de Werf F, Wallentin L Dabigatran vs. placebo in patients with acute coronary syndromes on dual antiplatelet therapy: a randomized, double-blind, phase II trial. *Eur Heart J* 2011 Nov;32:2781-9 [[21551462](#)]

#### **MDPIT, 1988:**

The effect of diltiazem on mortality and reinfarction after myocardial infarction. The Multicenter Diltiazem Postinfarction Trial Research Group *N Engl J Med* 1988;319:385-92 [[2899840](#)]

Bigger JT Jr, Coromilas J, Rolnitzky LM, Fleiss JL, Kleiger RE Effect of diltiazem on cardiac rate and rhythm after myocardial infarction. Multicenter Diltiazem Postinfarction Trial Investigators *Am J Cardiol* 1990;65:539-46 [[2178379](#)]

Moss AJ, Oakes D, Rubison M, McDermott M, Carleen E, Eberly S, Brown M Effects of diltiazem on long-term outcome after acute myocardial infarction in patients with and without a history of systemic hypertension. The Multicenter Diltiazem Postinfarction Trial Research Group *Am J Cardiol* 1991;68:429-33 [[1872266](#)]



Gibson RS, Hansen JF, Messerli F, Schechtman KB, Boden WE Long-term effects of diltiazem and verapamil on mortality and cardiac events in non-Q-wave acute myocardial infarction without pulmonary congestion: post hoc subset analysis of the multicenter diltiazem postinfarction trial and the second danish verapamil infarction trial studies Am J Cardiol 2000;86:275-9 [10922432]

#### **PARIS, 1980:**

, Persantine and aspirin in coronary heart disease. The Persantine-Aspirin Reinfarction Study Research Group. Circulation 1980; 62:449-61 [7398002]

, Persantine and aspirin in coronary heart disease. The Persantine-Aspirin Reinfarction Study Research Group. Circulation 1980; 62:449-61 [7398002]

#### **PARIS-II, 1986:**

Klimt CR, Knatterud GL, Stamler J, Meier P, Persantine-Aspirin Reinfarction Study. Part II. Secondary coronary prevention with persantine and aspirin. J Am Coll Cardiol 1986; 7:251-69 [2868029]

#### **CAMIAT , 1991:**

Cairns JA, Connolly SJ, Gent M, Roberts R Post-myocardial infarction mortality in patients with ventricular premature depolarizations. Canadian Amiodarone Myocardial Infarction Arrhythmia Trial Pilot Study. Circulation 1991;84:550-7 [1860199]

#### **Ceremuzynski, 1992:**

Ceremuzynski L, Kleczar E, Krzeminska-Pakula M, Kuch J, Nartowicz E, Smielak-Korombel J, Dyduszynski A, Maciejewicz J, Zaleska T, Lazarczyk-Kedzia E Effect of amiodarone on mortality after myocardial infarction: a double-blind, placebo-controlled, pilot study. J Am Coll Cardiol 1992;20:1056-62 [1401602]

#### **Hockings, 1987:**

Hockings BE, George T, Mahrous F, Taylor RR, Hajar HA Effectiveness of amiodarone on ventricular arrhythmias during and after acute myocardial infarction. Am J Cardiol 1987;60:967-70 [3673913]

#### **CARE, 1996:**

Sacks FM, Pfeffer MA, Moye LA, Rouleau JL, Rutherford JD, Cole TG, Brown L, Warnica JW, Arnold JM, Wun CC, Davis BR, Braunwald E, The effect of pravastatin on coronary events after myocardial infarction in patients with average cholesterol levels. Cholesterol and Recurrent Events Trial investigators. N Engl J Med 1996; 335:1001-9 [8801446]

Plehn JF, Davis BR, Sacks FM, Rouleau JL, Pfeffer MA, Bernstein V, Cuddy TE, Moy LA, Piller LB, Rutherford J, Simpson LM, Braunwald E Reduction of stroke incidence after myocardial infarction with pravastatin: the Cholesterol and Recurrent Events (CARE) study. The Care Investigators. Circulation 1999;99:216-23 [9892586]

#### **LIPID, 1998:**

, Prevention of cardiovascular events and death with pravastatin in patients with coronary heart disease and a broad range of initial cholesterol levels. The Long-Term Intervention with Pravastatin in Ischaemic Disease (LIPID) Study Group. N Engl J Med 1998; 339:1349-57 [9841303]

, Long-term effectiveness and safety of pravastatin in 9014 patients with coronary heart disease and average cholesterol concentrations: the LIPID trial follow-up. Lancet 2002; 359:1379-87 [11978335]

Design features and baseline characteristics of the LIPID (Long-Term Intervention with Pravastatin in Ischemic Disease) Study: a randomized trial in patients with previous acute myocardial infarction and/or unstable angina pectoris. Am J Cardiol 1995;76:474-9 [7653447]

#### **PACT, 2004:**

Thompson PL, Meredith I, Amerena J, Campbell TJ, Sloman JG, Harris PJ Effect of pravastatin compared with placebo initiated within 24 hours of onset of acute myocardial infarction or unstable angina: the Pravastatin in Acute Coronary Treatment (PACT) trial. Am Heart J 2004;148:e2 [15215811]

#### **4S, 1994:**

, Randomised trial of cholesterol lowering in 4444 patients with coronary heart disease: the Scandinavian Simvastatin Survival Study (4S) Lancet 1994; 344:1383-9 [7968073]

#### **DAVIT I, 1984:**

Verapamil in acute myocardial infarction. The Danish Study Group on Verapamil in Myocardial Infarction Eur Heart J 1984;5:516-28 [6383832]

Hansen JF Treatment with verapamil after an acute myocardial infarction. Review of the Danish studies on verapamil in myocardial infarction (DAVIT I and II) Drugs 1991;42 Suppl 2:43-53 [1718701]

#### **DAVIT II, 1990:**

Effect of verapamil on mortality and major events after acute myocardial infarction (the Danish Verapamil Infarction Trial II-DAVIT II) Am J Cardiol 1990;66:779-85 [2220572]

Vaage-Nilsen M, Rasmussen V Effect of verapamil on heart rate variability after an acute myocardial infarction. Danish Verapamil Infarction Trial II Cardiovasc Drugs Ther 1998;12:285-90 [9784908]

Vaage-Nilsen M, Rasmussen V, Hansen JF, Hagerup L, Sorensen MB, Pedersen-Bjergaard O, Mellemegaard K, Hollander NH, Nielsen I, Sigurd BM Effect of verapamil on arrhythmias and heart rate during 16 months following an acute myocardial infarction. The Danish Study Group on Verapamil in Myocardial Infarction Cardiovasc Drugs Ther 1994;8:147-51 [8086325]

**CRIS, 1996:**

Rengo F, Carbonin P, Pahor M, DeCaprio L, Bernabei R, Ferrara N, Carosella L, Acanfora D, Parlati S, Vitale D A controlled trial of verapamil in patients after acute myocardial infarction: results of the calcium antagonist reinfarction Italian study (CRIS) Am J Cardiol 1996;77:365-9 [8602564]

Ferrara N Giorn geront 1996;44:577-583

**Danish study, 1984:**

Verapamil in acute myocardial infarction. The Danish Study Group on Verapamil in Myocardial Infarction. Eur Heart J 1984;5:516-28 [6383832]

**PEGASUS 60mg, 2015:**

Bonaca MP, Bhatt DL, Braunwald E, Cohen M, Steg PG, Storey RF, Held P, Jensen EC, Sabatine MS Design and rationale for the Prevention of Cardiovascular Events in Patients With Prior Heart Attack Using Ticagrelor Compared to Placebo on a Background of Aspirin-Thrombolysis in Myocardial Infarction 54 (PEGASUS-TIMI 54) trial. Am Heart J 2014;167:437-444.e5 [24655690]

Bonaca MP, Bhatt DL, Cohen M, Steg PG, Storey RF, Jensen EC, Magnani G, Bansilal S, Fish MP, Im K, Bengtsson O, Ophuis TO, Budaj A, Theroux P, Ruda M, Hamm C, Goto S, Spinar J, Nicolau JC, Kiss RG, Murphy SA, Wiviott SD, Held P, Braunwald E, Sabatine MS Long-Term Use of Ticagrelor in Patients with Prior Myocardial Infarction. N Engl J Med 2015 Mar 14;: [25773268] 10.1056/NEJMoa1500857

**PEGASUS 90mg, 2015:**

Bonaca MP, Bhatt DL, Braunwald E, Cohen M, Steg PG, Storey RF, Held P, Jensen EC, Sabatine MS Design and rationale for the Prevention of Cardiovascular Events in Patients With Prior Heart Attack Using Ticagrelor Compared to Placebo on a Background of Aspirin-Thrombolysis in Myocardial Infarction 54 (PEGASUS-TIMI 54) trial. Am Heart J 2014;167:437-444.e5 [24655690]

Bonaca MP, Bhatt DL, Cohen M, Steg PG, Storey RF, Jensen EC, Magnani G, Bansilal S, Fish MP, Im K, Bengtsson O, Ophuis TO, Budaj A, Theroux P, Ruda M, Hamm C, Goto S, Spinar J, Nicolau JC, Kiss RG, Murphy SA, Wiviott SD, Held P, Braunwald E, Sabatine MS Long-Term Use of Ticagrelor in Patients with Prior Myocardial Infarction. N Engl J Med 2015 Mar 14;: [25773268] 10.1056/NEJMoa1500857

**TRA-2P TIMI 50, 2012:**

Morrow DA, Scirica BM, Fox KA, Berman G, Strony J, Veltri E, Bonaca MP, Fish P, McCabe CH, Braunwald E Evaluation of a novel antiplatelet agent for secondary prevention in patients with a history of atherosclerotic disease: design and rationale for the Thrombin-Receptor Antagonist in Secondary Prevention of Atherothrombotic Ischemic Events (TRA 2 degrees P)-TIMI 50 trial. Am Heart J 2009 Sep;158:335-341.e3 [19699854]

Morrow DA, Braunwald E, Bonaca MP, Ameriso SF, Dalby AJ, Fish MP, Fox KA, Lipka LJ, Liu X, Nicolau JC, Oude Ophuis AJ, Paolasso E, Scirica BM, Spinar J, Theroux P, Wiviott SD, Strony J, Murphy SA Vorapaxar in the Secondary Prevention of Atherothrombotic Events. N Engl J Med 2012 Mar 24;: [22443427] 10.1056/NEJMoa1200933

Scirica BM, Bonaca MP, Braunwald E, De Ferrari GM, Isaza D, Lewis BS, Mehrhof F, Merlini PA, Murphy SA, Sabatine MS, Tendera M, Van de Werf F, Wilcox R, Morrow DA Vorapaxar for secondary prevention of thrombotic events for patients with previous myocardial infarction: a prespecified subgroup analysis of the TRA 2P-TIMI 50 trial. Lancet 2012;380:1317-24 [22932716]

**Williams, 1997:**

Williams MJ, Morison IM, Parker JH, Stewart RA Progression of the culprit lesion in unstable coronary artery disease with warfarin and aspirin versus aspirin alone: preliminary study. J Am Coll Cardiol 1997;30:364-9 [9247506]

**EPSIM, 1982:**

A controlled comparison of aspirin and oral anticoagulants in prevention of death after myocardial infarction. N Engl J Med 1982;307:701-8 [7050710]

**ASPECT-2 (coumadin alone), 2002:**

van Es RF, Jonker JJ, Verheugt FW, Deckers JW, Grobbee DE Aspirin and coumadin after acute coronary syndromes (the ASPECT-2 study): a randomised controlled trial. Lancet 2002;360:109-13 [12126819]

**PARIS, 1980:**

, Persantine and aspirin in coronary heart disease. The Persantine-Aspirin Reinfarction Study Research Group. Circulation 1980; 62:449-61 [7398002]

**WARIS II (warfarin alone), 2002:**

Hurlen M, Abdelnoor M, Smith P, Erikssen J, Arnesen H Warfarin, aspirin, or both after myocardial infarction. N Engl J Med 2002;347:969-74 [[12324552](#)]

**TNT, 2005:**

LaRosa JC, Grundy SM, Waters DD, Shear C, Barter P, Fruchart JC, Gotto AM, Greten H, Kastelein JJ, Shepherd J, Wenger NK Intensive lipid lowering with atorvastatin in patients with stable coronary disease. N Engl J Med 2005 Apr 7;352:1425-35 [[15755765](#)]

Wenger NK, Lewis SJ, Welty FK, Herrington DM, Bittner V Beneficial effects of aggressive low-density lipoprotein cholesterol lowering in women with stable coronary heart disease in the Treating to New Targets (TNT) study. Heart 2008;94:434-9 [[18070940](#)]

Johnson C, Waters DD, DeMicco DA, Breazna A, Bittner V, Greten H, Grundy SM, LaRosa JC Comparison of effectiveness of atorvastatin 10 mg versus 80 mg in reducing major cardiovascular events and repeat revascularization in patients with previous percutaneous coronary intervention (post hoc analysis of the Treating to New Targets [TNT] Study). Am J Cardiol 2008;102:1312-7 [[18993147](#)]

Waters DD, Guyton JR, Herrington DM, McGowan MP, Wenger NK, Shear C Treating to New Targets (TNT) Study: does lowering low-density lipoprotein cholesterol levels below currently recommended guidelines yield incremental clinical benefit? Am J Cardiol 2004;93:154-8 [[14715339](#)]

**Vascular basis, 2005:**

Stone PH, Lloyd-Jones DM, Kinlay S, Frei B, Carlson W, Rubenstein J, Andrews TC, Johnstone M, Sopko G, Cole H, Orav J, Selwyn AP, Creager MA Effect of intensive lipid lowering, with or without antioxidant vitamins, compared with moderate lipid lowering on myocardial ischemia in patients with stable coronary artery disease: the Vascular Basis for the Treatment of Myocardial Ischemia Study. Circulation 2005;111:1747-55 [[15809368](#)]

**Tuttle, 2008:**

Tuttle KR, Shuler LA, Packard DP, Milton JE, Daratha KB, Bibus DM, Short RA Comparison of low-fat versus Mediterranean-style dietary intervention after first myocardial infarction (from The Heart Institute of Spokane Diet Intervention and Evaluation Trial). Am J Cardiol 2008;101:1523-30 [[18489927](#)]

## 4 cardiovascular prevention

Trial	Treatments	Patients	Trials design and methods
<b>evolocumab vs</b>			
<a href="#">Mendel 1 , 2012</a> [NCT01375777] n=NA follow-up:	-	-	
<a href="#">MENDEL 2</a> [NCT01763827] n=NA	-	-	
<a href="#">YUKAWA-1 , 2014</a> n=NA follow-up:	-	-	
<b>rivaroxaban vs aspirin</b>			
<a href="#">COMPASS (rivaroxaban alone) , 2017</a> [NCT01776424] n=27400 follow-up:	Rivaroxaban 2.5 mg twice daily alone versus aspirin 100 mg once daily	Patients With Coronary or Peripheral Artery Disease	
<b>rivaroxaban + aspirin vs aspirin</b>			

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>COMPASS (rivaroxaban + aspirin) , 2017</b> [NCT01776424] n=9152/9126 follow-up: 23 months	rivaroxaban (2.5 mg twice daily) plus aspirin (100 mg once daily) versus aspirin 100 mg once daily	Patients With Coronary or Peripheral Artery Disease	Parallel groups double-blind
<b>ticagrelor vs clopidogrel</b>			
<b>EUCLID , 2016</b> [NCT01732822] n=NA follow-up: 30 months (median)	ticagrelor (90 mg twice daily) versus clopidogrel (75 mg once daily)	patients with symptomatic peripheral artery disease	
<b>cholestyramine vs control</b>			
<b>STARS (cholestyramine) , 1992</b> n=30/30 follow-up: 3 years	cholestyramine versus diet	patients with angina or past myocardial infarction	
<b>dipyridamol vs control</b>			
<b>Atlanta (Sbar) , 1967</b> n=30/30 follow-up: 6 months	dipyridamole 150mg daily versus placebo	patients with angina pectoris	parallel groups double-blind
<b>Wirecki , 1967</b> n=28/28 follow-up: 7 months	dipyridamole 150mg daily versus placebo	patients with angina pectoris	parallel groups double blind
<b>Becker , 1967</b> n=14/13 follow-up: 5 months	dipyridamole 225mg daily versus placebo	-	parallel groups double-blind
<b>folic acid vs control</b>			
<b>FOLARDA (Liem) , 2004</b> n=140/143 follow-up: 1 year	folic acid 5 mg per day for 1 year versus usual care	patients with acute MI and total cholesterol >6.5 mmol/l	Parallel groups open The Netherlands
<b>GOES (Liem) , 2003</b> n=300/293 follow-up: 24 months	folic acid 0.5 mg per day versus usual care	patients with stable coronary artery disease	Parallel groups open The Netherlands
<b>folic acid, B12 vs control</b>			
<b>NORVIT (folic acid + B12) (Bonaa) , 2006</b> [NCT00266487] n=1872/1877 follow-up: 36 months	folic acid 0.8mg and B12 0.4 mg daily versus no folic acid and B12	men and women who had had an acute myocardial infarction within seven days before	Factorial plan double-blind Norway
<b>folic acid, vit B12 and vit B6 vs control</b>			

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>NORVIT (folic acid, B12 and vit B6) (Bonnae) , 2006</b> [NCT00266487] n=937/943 follow-up: 36 months	0.8 mg of folic acid, 0.4 mg of vitamin B12, and 40 mg of vitamin B6 versus placebo	men and women who had had an acute myocardial infarction within seven days	Factorial plan double-blind Norway
<b>MaxEPA vs control</b>			
<b>Bellamy , 1992</b> n=60/60 follow-up: 7 months	MaxEPA capsules (3g/d EPA + DHA) versus no treatment	people referred for coronary angioplasty	Parallel groups NA UK
<b>Dehmer , 1998</b> n=46/44 follow-up: 6 months	MaxEPA capsules, 18/d (5.4g EPA + DHA daily) versus no treatment	men undergoing coronary angioplasty imag	open US
<b>Kaul , 1992</b> n=58/49 follow-up: 6 months	MaxEPA capsules, 10/d (3g/d EPA + DHA) versus no treatment	people undergoing angioplasty	Parallel groups open India
<b>Mediterranean diet vs control</b>			
<b>Lyon</b> n=302/303 follow-up:	-	-	
<b>Mediterranean diet with EOVV vs control</b>			
<b>PREDIMED (olive oil) , 2013</b> [ISRCTN35739639] n=2543/2450 follow-up: 4.8 years	Mediterranean diet supplemented with extra-virgin olive oil versus control diet (advice to reduce dietary fat)	participants who were at high cardiovascular risk, but with no cardiovascular disease	Parallel groups open Spain
<b>Mediterranean diet with nuts vs control</b>			
<b>PREDIMED (nuts) , 2013</b> [ISRCTN35739639] n=2454/2450 follow-up: 4.8 years	Mediterranean diet supplemented with mixed nuts versus control diet (advice to reduce dietary fat)	participants who were at high cardiovascular risk, but with no cardiovascular disease	open Spain
<b>Multiple risk factor interventions vs control</b>			
<b>CELL , 1995</b> n=339/320 follow-up: 18 months	intensive" health care advice through six group sessions versus usual care	subjects aged 30-59 years, with at least two cardiovascular risk factors in addition to moderately high lipid concentrations: total cholesterol $\geq$ 6.5 mmol/l on three occasions, triglycerides $<$ 4.0 mmol/l, and ratio of low density lipoprotein cholesterol to high density lipoprotein cholesterol $>$ 4.0	Factorial plan open

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>Family Heart , 1994</b> n=3436/5912 follow-up: 1 y	Nurse led programme using a family centred approach with follow up according to degree of risk. Counselling on diet, weight, smoking, exercise, alcohol versus control	men aged 40-59 and their partners	Parallel groups double-blind UK
<b>Gteborg Study , 1986</b> n=10004/20018 follow-up: 11.8 yr	multifactorial intervention programme on coronary heart disease versus no intervention	random sample of men age 47-55 y	open Sweden
<b>HDFP , 1979</b> [NCT00000498] n=5485/5455 follow-up: 5 yr	Stepped care: Antihypertensive drugs, diet, smoking advice, weight control, exercise versus usual primary care	persons with high blood pressure	Parallel groups open USA
<b>Helsinki Businessmen Study , 1985</b> n=612/610 follow-up: 5 yr	Multifactorial prevention of cardiovascular diseases versus no intervention	healthy men 40-58 y at high risk	Parallel groups open Finland
<b>Johns Hopkins , 1983</b> n=350/50 follow-up: 5 yr	health education interventions versus control	hypertensives men and women	Factorial plan open USA
<b>Meland , 1997</b> n=69/58 follow-up: 1 y	patient-centred, self-directive intervention of lifestyle changes in general practice versus conventional care	men with high coronary heart disease risk	Parallel groups open
<b>MRFIT , 1982</b> [NCT00000487?acronym=] n=6428/6438 follow-up: 6 yr	special intervention (SI) program consisting of stepped-care treatment for hypertension, counseling for cigarette smoking, and dietary advice for lowering blood cholesterol levels versus no intervention	high-risk men aged 35 to 57 years	Parallel groups open
<b>Oslo , 1981</b> n=612/610 follow-up: 5 yr	recommendation to lower their blood lipids by change of diet and to stop smoking versus no intervention	healthy, normotensive men at high risk of coronary heart disease	Parallel groups open Oslo, Norway
<b>OXCHECK , 1994</b> n=8307/2783 follow-up: 3 yr	health checks by nurses versus no intervention	patients from general practice aged 35-64 years	Parallel groups open UK

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>WHO Factories , 1982</b> n=30489/26971 follow-up: 6 years	multifactorial prevention of coronary heart disease versus no intervention	men employed in 80 factories in Belgium, Italy, Poland, and the UK	Parallel groups open Belgium, Italy, Poland, and the UK
<b>niacin vs control</b>			
<b>VA drugs , 1968</b> n=77/143 follow-up: 3.2 years	-	-	Parallel groups double blind
<b>niacin+colestipol vs control</b>			
<b>UCSF SCOR , 1990</b> n=72 follow-up: 26 months	Niacin 07.5 g colestipol 1520 g versus Conventional therapy	patients with heterozygous familial hypercholesterolemia	
<b>Omacor vs control</b>			
<b>Eritslund , 1996</b> n=317/293 follow-up: 12 months	Omacor capsules, 4/d (3.3g EPA + DHA daily) versus no treatment	people admitted for coronary bypass grafting	Parallel groups open Norway
<b>GISSI-P , 1999</b> n=5665/5668 follow-up: median 40 months	Omacor gelatine capsules, 1/d (0.9g/d EPA + DHA daily) versus no treatment	people with recent myocardial infarction	Parallel groups open Italy
<b>omega-3 Fatty acids vs control</b>			
<b>OMEGA , 2009</b> [NCT00251134] n=1940/1911 follow-up: 1 year	omega-3 fatty acids 1g daily (and standard medical therapy) versus standard medical therapy alone	Patients within 3-14 days after a non-ST-elevation myocardial infarction (NSTEMI) or ST-elevation myocardial infarction (STEMI)	Parallel groups open Germany
<b>policosanol vs control</b>			
<b>Batista , 1996</b> n=15/14 follow-up: 1.7 years	-	-	Parallel groups
<b>Castano , 2001</b> n=27/29 follow-up: 2 years	policosanol 10 mg twice daily versus placebo	intermittent claudication	Parallel groups double-blind
<b>Ms , 1999</b> n=219/218 follow-up: 24 weeks	policosanol 5mg titrated up for 10mg daily versus placebo	patients with type II hypercholesterolemia and additional coronary risk factors	Parallel groups double-blind
<b>pravastatin vs control</b>			
<b>FAST Fukuoka pravastatin , 2002</b> n=83/81 follow-up: 2 years	pravastatin 10 mg/day versus control group (diet alone)	asymptomatic hypercholesterolemic patients	open Japan

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>MEGA , 2006</b> [NCT00211705] n=3866/3966 follow-up: 5.3 y	pravastatin 10 mg daily (20 mg per day if the total cholesterol concentration did not decrease to 569 mmol/L or less) versus control	patients with hypercholesterolaemia (total cholesterol 569698 mmol/L) and no history of coronary heart disease or stroke	Parallel groups open, blind assessment Japan
<b>Promega vs control</b>			
<b>Milner , 1989</b> n=100/100 follow-up: 6 months	Promega 9 capsules/d (4.5g EPA + DHA) versus no treatment	people about to undergo angioplasty	Parallel groups open with blind assessment US
<b>simvastatin vs control</b>			
<b>Hong , 2005</b> n=106/96 follow-up: 1 year	simvastatin versus no treatment	patients with ischemic heart failure who underwent percutaneous coronary intervention (PCI) for acute myocardial infarction (left ventricular [LV] ejection fraction <40% )	Parallel groups open
<b>vitamin E vs control</b>			
<b>GISSI , 1999</b> n=5660/5664 follow-up: 3.5y	vitamin E 300mg/d versus no vitamine E	patients with recent (3 months) myocardial infarction	Factorial plan open Italy
<b>PPP , 2001</b> n=2231/2264 follow-up: 3.6y	vitamin E (300 mg/day) versus no vitamin E	men and women aged 50 years or greater, with at least one of the major recognised cardiovascular risk factors	Factorial plan open Italy
<b>intensive lipid-lowering therapy vs diet</b>			
<b>FATS , 1990</b> [NCT00000512] n=94/52 follow-up: 2.5 years	intensive lipid-lowering therapy with various drugs versus placebo	men no more than 62 years of age who had apolipoprotein B levels greater than or equal to 125 mg per deciliter, documented coronary artery disease, and a family history of vascular disease	Parallel groups open Japan
<b>alirocumab vs ezetimibe (on top statin)</b>			
<b>ODYSSEY OPTIONS I</b> n=NA follow-up: 24 wk	Alirocumab 75 mg with potential up-titration to 150 mg Q2W versus Ezetimibe 10 mg	high-cardiovascular-risk patients with hypercholesterolemia not adequately controlled with atorvastatin (20 or 40 mg) or rosuvastatin (10 or 20 mg)	
<b>ODYSSEY OPTIONS II</b> n=NA follow-up: 24 wk	Alirocumab 75 mg with potential up-titration to 150 mg Q2W versus Ezetimibe 10 mg	high-cardiovascular-risk patients with hypercholesterolemia not adequately controlled with atorvastatin (20 or 40 mg) or rosuvastatin (10 or 20 mg)	
<b>alirocumab vs ezetimibe alone</b>			

continued...



<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>ODYSSEY MONO</b> [NCT01644474] n=NA follow-up: 24 wk	Alirocumab 75 mg Q2W versus Ezetimibe 10 mg	hypercholesterolemic patients at moderate cardiovascular risk not receiving statins or other lipid-lowering therapy	double-blind
<b>evolocumab vs ezetimibe alone</b>			
<b>GAUSS 2</b> [NCT01763905] n=102/205 follow-up:	evolocumab 140 mg every two weeks (Q2W) or evolocumab 420 mg once monthly (QM) versus ezetimibe 10 mg	patients with statin intolerance	
<b>anticoagulant vs no anticoagulant</b>			
<b>MacMillan , 1960</b> n=NA	-	-	
<b>Borchegrevink , 1960</b> n=NA	-	-	
<b>Clausen , 1961</b> n=NA	-	-	
<b>Harvald , 1961</b> n=NA	-	-	
<b>Conrad , 1964</b> n=NA	-	-	
<b>Wasserman , 1966</b> n=NA	-	-	
<b>Loeliger , 1967</b> n=NA	-	-	
<b>Lovell , 1967</b> n=NA	-	-	
<b>Seaman , 1969</b> n=NA	-	-	
<b>Sorensen , 1969</b> n=NA	-	-	
<b>Meuwisse , 1969</b> n=NA	-	-	
<b>Drapkin and Merskey , 1972</b> n=NA	-	-	
<b>dicoumarol vs no anticoagulant</b>			
<b>Apenstrom and Korsan-Bengtson , 1964</b> n=NA follow-up:	-	-	
<b>any statin vs no statin</b>			

continued...

Trial	Treatments	Patients	Trials design and methods
Sakamoto , 2006 n=241/245 follow-up: up to 24 months	any available statin versus no statin	Japanese patients with AMI within 96 hours of AMI onset	Parallel groups open Japan

More details and results :

- cholesterol lowering intervention for cardiovascular prevention in patients with LDL elevation and without CHD at <http://www.trialresultscenter.org/go-Q5>
- cholesterol lowering intervention for cardiovascular prevention in diabetic patients at <http://www.trialresultscenter.org/go-Q6>
- cholesterol lowering intervention for cardiovascular prevention in elderly at <http://www.trialresultscenter.org/go-Q7>
- cholesterol lowering intervention for cardiovascular prevention in high risk patients with or without LDL cholesterol elevation at <http://www.trialresultscenter.org/go-Q11>
- cholesterol lowering intervention for cardiovascular prevention in patients with prior MI or with CHD at <http://www.trialresultscenter.org/go-Q12>
- omega-3 fatty acids for cardiovascular prevention in all type of patients at <http://www.trialresultscenter.org/go-Q121>
- omega-3 fatty acids for cardiovascular prevention in patients at high risk at <http://www.trialresultscenter.org/go-Q123>
- omega-3 fatty acids for cardiovascular prevention in patients at low risk at <http://www.trialresultscenter.org/go-Q124>
- cholesterol lowering intervention for cardiovascular prevention in patients with other atherosclerotic localisation at <http://www.trialresultscenter.org/go-Q126>
- plasma homocysteine lowering intervention for cardiovascular prevention in all type of patients at <http://www.trialresultscenter.org/go-Q127>
- antioxydants for cardiovascular prevention in all type of patients at <http://www.trialresultscenter.org/go-Q131>
- cholesterol lowering intervention for cardiovascular prevention in patient with related disease at <http://www.trialresultscenter.org/go-Q137>
- cholesterol lowering intervention for cardiovascular prevention in all chronic situations at <http://www.trialresultscenter.org/go-Q154>
- cholesterol lowering intervention for cardiovascular prevention in post stroke (or TIA) at <http://www.trialresultscenter.org/go-Q155>
- antiplatelets drug for cardiovascular prevention in diabetic patients at <http://www.trialresultscenter.org/go-Q220>
- antiplatelets drug for cardiovascular prevention in all type of patients at <http://www.trialresultscenter.org/go-Q226>
- antioxydants for cardiovascular prevention in diabetic patients at <http://www.trialresultscenter.org/go-Q232>
- cholesterol lowering intervention for cardiovascular prevention in primary prevention at <http://www.trialresultscenter.org/go-Q241>
- antiplatelets drug for cardiovascular prevention in secondary prevention in patients with intermittent claudication at <http://www.trialresultscenter.org/go-Q275>
- antiplatelets drug for cardiovascular prevention in secondary prevention in patients with CAD at <http://www.trialresultscenter.org/go-Q276>

## References

### Mendel 1, 2012:

Koren MJ, Scott R, Kim JB, Knusel B, Liu T, Lei L, Bolognese M, Wasserman SM Efficacy, safety, and tolerability of a monoclonal antibody to proprotein convertase subtilisin/kexin type 9 as monotherapy in patients with hypercholesterolaemia (MENDEL): a randomised, double-blind, placebo-controlled, phase 2 study. *Lancet* 2012 Dec 8;380:1995-2006 [23141812] 10.1016/S0140-6736(12)61771-1

### MENDEL 2, :

### YUKAWA-1, 2014:

Hirayama A, Honarpour N, Yoshida M, Yamashita S, Huang F, Wasserman SM, Teramoto T Effects of evolocumab (AMG 145), a monoclonal antibody to PCSK9, in hypercholesterolemic, statin-treated Japanese patients at high cardiovascular risk—primary results from the phase 2 YUKAWA study. *Circ J* 2014;78:1073-82 [24662398]

**COMPASS (rivaroxaban alone), 2017:**

**COMPASS (rivaroxaban + aspirin), 2017:**

Eikelboom JW, Connolly SJ, Bosch J, Dagenais GR, Hart RG, Shestakovska O, Diaz R, Alings M, Lonn EM, Anand SS, Widimsky P, Hori M, Avezum A, Piegas LS, Branch KRH, Probstfield J, Bhatt DL, Zhu J, Liang Y, Maggioni AP, Lopez-Jaramillo P, O'Donnell M, Kakka Rivaroxaban with or without Aspirin in Stable Cardiovascular Disease. *N Engl J Med* 2017;377:1319-1330 [28844192]

**EUCLID, 2016:**

Jones WS, Baumgartner I, Hiatt WR, Heizer G, Conte MS, White CJ, Berger JS, Held P, Katona BG, Mahaffey KW, Norgren L, Blomster J, Millegrd M, Reist C, Patel MR, Fowkes GR Ticagrelor Compared With Clopidogrel in Patients with Prior Lower Extremity Revascularization for Peripheral Artery Disease. *Circulation* 2016 Nov 13; [27840336] 10.1161/CIRCULATIONAHA.116.025880

Hiatt WR, Fowkes FG, Heizer G, Berger JS, Baumgartner I, Held P, Katona BG, Mahaffey KW, Norgren L, Jones WS, Blomster J, Millegrd M, Reist C, Patel MR Ticagrelor versus Clopidogrel in Symptomatic Peripheral Artery Disease. *N Engl J Med* 2017;376:32-40 [27959717]

**STARS (cholestyramine), 1992:**

Watts GF, Lewis B, Brunt JN, Lewis ES, Coltart DJ, Smith LD, Mann JI, Swan AV Effects on coronary artery disease of lipid-lowering diet, or diet plus cholestyramine, in the St Thomas' Atherosclerosis Regression Study (STARS) *Lancet* 1992;339:563-9 [1347091]

**Atlanta (Sbar), 1967:**

Sbar S, Schlant RC Dipyridamole in the treatment of angina pectoris. A double-blind evaluation. *JAMA* 1967;201:865-7 [5340622]

**Wirecki, 1967:**

Wirecki M Treatment of angina pectoris with dipyridamole: a long-term double blind study. *J Chronic Dis* 1967;20:139-45 [5336520]

**Becker, 1967:**

Becker MC. Angina pectoris: A double blind study with dipyridamole *Journal of the Newark Beth Israel Hospital* 1967;18:88-94

**FOLARDA (Liem), 2004:**

Liem AH, van Boven AJ, Veeger NJ, Withagen AJ, Robles de Medina RM, Tijssen JG, van Veldhuisen DJ Efficacy of folic acid when added to statin therapy in patients with hypercholesterolemia following acute myocardial infarction: a randomised pilot trial. *Int J Cardiol* 2004;93:175-9 [14975544] 10.1016/j.ijcard.2003.02.001

**GOES (Liem), 2003:**

Liem A, Reynierse-Buitenwerf GH, Zwinderman AH, Jukema JW, van Veldhuisen DJ Secondary prevention with folic acid: effects on clinical outcomes. *J Am Coll Cardiol* 2003;41:2105-13 [12821232]

Liem A, Reynierse-Buitenwerf GH, Zwinderman AH, Jukema JW, van Veldhuisen DJ Secondary prevention with folic acid: results of the Goes extension study. *Heart* 2005;91:1213-4 [16103563] 10.1136/hrt.2004.035030

**NORVIT (folic acid + B12) (Bonaa), 2006:**

Bnaa KH, Njlstad I, Ueland PM, Schirmer H, Tverdal A, Steigen T, Wang H, Nordrehaug JE, Arnesen E, Rasmussen K Homocysteine lowering and cardiovascular events after acute myocardial infarction. *N Engl J Med* 2006;354:1578-88 [16531614] 10.1056/NEJMoa055227

**NORVIT (folic acid, B12 and vit B6) (Bonaa), 2006:**

Bnaa KH, Njlstad I, Ueland PM, Schirmer H, Tverdal A, Steigen T, Wang H, Nordrehaug JE, Arnesen E, Rasmussen K Homocysteine lowering and cardiovascular events after acute myocardial infarction. *N Engl J Med* 2006;354:1578-88 [16531614] 10.1056/NEJMoa055227

**Bellamy, 1992:**

Bellamy CM, Schofield PM, Faragher EB, Ramsdale DR Can supplementation of diet with omega-3 polyunsaturated fatty acids reduce coronary angioplasty restenosis rate? *Eur Heart J* 1992 Dec;13:1626-31 [1289091]

**Dehmer, 1998:**

Dehmer GJ, Popma JJ, van den Berg EK, Eichhorn EJ, Prewitt JB, Campbell WB, Jennings L, Willerson JT, Schmitz JM Reduction in the rate of early restenosis after coronary angioplasty by a diet supplemented with n-3 fatty acids. *N Engl J Med* 1988 Sep 22;319:733-40 [2842680]

**Kaul, 1992:**

Kaul U, Sanghvi S, Bahl VK, Dev V, Wasir HS Fish oil supplements for prevention of restenosis after coronary angioplasty. *Int J Cardiol* 1992 Apr;35:87-93 [1563884]

**Lyon, :**

de Lorgeril M, Renaud S, Mamelle N, Salen P, Martin JL, Monjaud I, Guidollet J, Touboul P, Delaye J Mediterranean alpha-linolenic acid-rich diet in secondary prevention of coronary heart disease. *Lancet* 1994;343:1454-9 [7911176]

De Lorgeril M, Salen P, Martin JL, Mamelle N, Monjaud I, Touboul P, Delaye J Effect of a mediterranean type of diet on the rate of cardiovascular complications in patients with coronary artery disease. Insights into the cardioprotective effect of certain nutriments. *J Am Coll Cardiol* 1996;28:1103-8 [8890801] [10.1016/S0735-1097\(96\)00280-X](#)

de Lorgeril M, Renaud S, Mamelle N, Salen P, Martin JL, Monjaud I, Guidollet J, Touboul P, Delaye J Mediterranean alpha-linolenic acid-rich diet in secondary prevention of coronary heart disease. *Lancet* 1994;343:1454-9 [7911176]

De Lorgeril M, Salen P, Martin JL, Mamelle N, Monjaud I, Touboul P, Delaye J Effect of a mediterranean type of diet on the rate of cardiovascular complications in patients with coronary artery disease. Insights into the cardioprotective effect of certain nutriments. *J Am Coll Cardiol* 1996;28:1103-8 [8890801] [10.1016/S0735-1097\(96\)00280-X](#)

#### **PREDIMED (olive oil), 2013:**

Estruch R, Ros E, Salas-Salvad J, Covas MI, D Pharm, Corella D, Ars F, Gmez-Gracia E, Ruiz-Gutierrez V, Fiol M, Lapetra J, Lamuela-Raventos RM, Serra-Majem L, Pint X, Basora J, Muñoz MA, Sorl JV, Martínez JA, Martínez-González MA Primary Prevention of Cardiovascular Disease with a Mediterranean Diet. *N Engl J Med* 2013 Feb 25;: [23432189] [10.1056/NEJMoa1200303](#)

#### **PREDIMED (nuts), 2013:**

Estruch R, Ros E, Salas-Salvad J, Covas MI, D Pharm, Corella D, Ars F, Gmez-Gracia E, Ruiz-Gutierrez V, Fiol M, Lapetra J, Lamuela-Raventos RM, Serra-Majem L, Pint X, Basora J, Muñoz MA, Sorl JV, Martínez JA, Martínez-González MA Primary Prevention of Cardiovascular Disease with a Mediterranean Diet. *N Engl J Med* 2013 Feb 25;: [23432189] [10.1056/NEJMoa1200303](#)

#### **CELL, 1995:**

Lindholm LH, Ekblom T, Dash C, Eriksson M, Tibblin G, Scherström B The impact of health care advice given in primary care on cardiovascular risk. *CELL Study Group. BMJ* 1995;310:1105-9 [7742677]

Lindholm LH, Ekblom T, Dash C, Isacson A, Scherström B Changes in cardiovascular risk factors by combined pharmacological and nonpharmacological strategies: the main results of the CELL Study. *J Intern Med* 1996;240:13-22 [8708586]

#### **Family Heart, 1994:**

Randomised controlled trial evaluating cardiovascular screening and intervention in general practice: principal results of British family heart study. *Family Heart Study Group. BMJ* 1994;308:313-20 [8124121]

#### **Gteborg Study, 1986:**

Wilhelmsen L, Berglund G, Elmfeldt D, Tibblin G, Wedel H, Pennert K, Vedin A, Wilhelmsson C, Werk L The multifactor primary prevention trial in Gteborg, Sweden. *Eur Heart J* 1986;7:279-88 [3720755]

#### **HDFP, 1979:**

Five-year findings of the hypertension detection and follow-up program. I. Reduction in mortality of persons with high blood pressure, including mild hypertension. *Hypertension Detection and Follow-up Program Cooperative Group. JAMA* 1979;242:2562-71 [490882]

#### **Helsinki Businessmen Study, 1985:**

Miettinen TA, Huttunen JK, Naukkarinen V, Strandberg T, Mattila S, Kumlin T, Sarna S Multifactorial primary prevention of cardiovascular diseases in middle-aged men. Risk factor changes, incidence, and mortality. *JAMA* 1985;254:2097-102 [4046137]

Strandberg TE, Salomaa VV, Naukkarinen VA, Vanhanen HT, Sarna SJ, Miettinen TA Long-term mortality after 5-year multifactorial primary prevention of cardiovascular diseases in middle-aged men. *JAMA* 1991;266:1225-9 [1870247]

Strandberg TE, Salomaa VV, Vanhanen HT, Naukkarinen VA, Sarna SJ, Miettinen TA Mortality in participants and non-participants of a multifactorial prevention study of cardiovascular diseases: a 28 year follow up of the Helsinki Businessmen Study. *Br Heart J* 1995;74:449-54 [7488463]

#### **Johns Hopkins, 1983:**

Morisky DE, Levine DM, Green LW, Shapiro S, Russell RP, Smith CR Five-year blood pressure control and mortality following health education for hypertensive patients. *Am J Public Health* 1983;73:153-62 [6849473]

#### **Meland, 1997:**

Meland E, Laerum E, Ulvik RJ Effectiveness of two preventive interventions for coronary heart disease in primary care. *Scand J Prim Health Care* 1997;15:57-64 [9101627]

Meland E, Maeland JG, Laerum E The importance of self-efficacy in cardiovascular risk factor change. *Scand J Public Health* 1999;27:11-7 [[10847665](#)]

#### **MRFIT, 1982:**

Mortality rates after 10.5 years for participants in the Multiple Risk Factor Intervention Trial. Findings related to a priori hypotheses of the trial. The Multiple Risk Factor Intervention Trial Research Group. *JAMA* 1990;263:1795-801 [[2179590](#)]

Multiple risk factor intervention trial. Risk factor changes and mortality results. Multiple Risk Factor Intervention Trial Research Group. *JAMA* 1982;248:1465-77 [[7050440](#)]

#### **Oslo, 1981:**

Anderssen S, Holme I, Urdal P, Hjerermann I Diet and exercise intervention have favourable effects on blood pressure in mild hypertensives: the Oslo Diet and Exercise Study (ODES). *Blood Press* 1995;4:343-9 [[8746601](#)]

Hjerermann I, Holme I, Leren P Oslo Study Diet and Antismoking Trial. Results after 102 months. *Am J Med* 1986;80:7-11 [[3511692](#)]

Hjerermann I, Velve Byre K, Holme I, Leren P Effect of diet and smoking intervention on the incidence of coronary heart disease. Report from the Oslo Study Group of a randomised trial in healthy men. *Lancet* 1981;2:1303-10 [[6118715](#)]

Holme I, Hjerermann I, Helgeland A, Leren P The Oslo Study: diet and antismoking advice. Additional results from a 5-year primary preventive trial in middle-aged men. *Prev Med* 1985;14:279-92 [[3903733](#)]

#### **OXCHECK, 1994:**

Effectiveness of health checks conducted by nurses in primary care: results of the OXCHECK study after one year. Imperial Cancer Research Fund OXCHECK Study Group. *BMJ* 1994;308:308-12 [[8124120](#)]

#### **WHO Factories, 1982:**

European collaborative trial of multifactorial prevention of coronary heart disease: final report on the 6-year results. World Health Organisation European Collaborative Group. *Lancet* 1986;1:869-72 [[2870351](#)]

Multifactorial trial in the prevention of coronary heart disease: 2. Risk factor changes at two and four years. *Eur Heart J* 1982;3:184-90 [[7084265](#)]

#### **VA drugs, 1968:**

Schoch HK. The US Veterans Administration Cardiology drug lipid study: an interim report *Adv Exp Med Biol.* 1968;4:405-420

#### **UCSF SCOR, 1990:**

Kane JP, Malloy MJ, Ports TA, Phillips NR, Diehl JC, Havel RJ Regression of coronary atherosclerosis during treatment of familial hypercholesterolemia with combined drug regimens. *JAMA* 1990;264:3007-12 [[2243428](#)]

#### **Eritsland, 1996:**

Eritsland J, Arnesen H, Gronseth K, Fjeld NB, Abdelnoor M Effect of dietary supplementation with n-3 fatty acids on coronary artery bypass graft patency. *Am J Cardiol* 1996 Jan 1;77:31-6 [[8540453](#)]

Eritsland J, Arnesen H, Seljeflot I, Hostmark AT Long-term metabolic effects of n-3 polyunsaturated fatty acids in patients with coronary artery disease. *Am J Clin Nutr* 1995 Apr;61:831-6 [[7702027](#)]

#### **GISSI-P, 1999:**

Dietary supplementation with n-3 polyunsaturated fatty acids and vitamin E after myocardial infarction: results of the GISSI-Prevenzione trial. Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto miocardico. *Lancet* 1999 Aug 7;354:447-55 [[10465168](#)]

Marchioli R, Barzi F, Bomba E, Chieffo C, Di Gregorio D, Di Mascio R, Franzosi MG, Geraci E, Levantesi G, Maggioni AP, Mantini L, Marfisi RM, Mastrogiuseppe G, Mininni N, Nicolosi GL, Santini M, Schweiger C, Tavazzi L, Tognoni G, Tucci C, Valagussa F Early protection against sudden death by n-3 polyunsaturated fatty acids after myocardial infarction: time-course analysis of the results of the Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto Miocardico (GISSI)-Prevenzione. *Circulation* 2002 Apr 23;105:1897-903 [[11997274](#)]

#### **OMEGA, 2009:**

Senges Randomized Trial of Omega-3 Fatty Acids on Top of Modern Therapy After Acute Myocardial Infarction: The OMEGA Trial ACC.09/i2, Orlando, FL, March 2009 [0]

Rauch B, Schiele R, Schneider S, Diller F, Victor N, Gohlke H, Gottwik M, Steinbeck G, Del Castillo U, Sack R, Worth H, Katus H, Spitzer W, Sabin G, Seneges J OMEGA, a randomized, placebo-controlled trial to test the effect of highly purified omega-3 fatty acids on top of modern guideline-adjusted therapy after myocardial infarction. *Circulation* 2010;122:2152-9 [[21060071](#)] [10.1161/CIRCULATIONAHA.110.948562](#)

#### **Batista, 1996:**

Batista JF, Stsler RJ, Padrn R, Sosa F, Pereztol O, Prez B.P Functional Improvement in Coronary Artery Disease After 20 months of Lipid-Lowering Therapy with Picosanol

Advances in Therapy. 1996;13:137-148imag

**Castano, 2001:**

Castao G, Ms Ferreira R, Fernndez L, Gmez R, Illnait J, Fernndez C A long-term study of picosanol in the treatment of intermittent claudication. Angiology 2001;52:115-25 [11228084]

**Ms, 1999:**

Ms R, Castao G, Illnait J, Fernndez L, Fernndez J, Alemn C, Pontigas V, Lescay M Effects of picosanol in patients with type II hypercholesterolemia and additional coronary risk factors. Clin Pharmacol Ther 1999;65:439-47 [10223782]

**FAST Fukuoka pravastatin, 2002:**

Sawayama Y, Shimizu C, Maeda N, Tatsukawa M, Kinukawa N, Koyanagi S, Kashiwagi S, Hayashi J Effects of probucol and pravastatin on common carotid atherosclerosis in patients with asymptomatic hypercholesterolemia. Fukuoka Atherosclerosis Trial (FAST). J Am Coll Cardiol 2002;39:610-6 [11849859]

**MEGA, 2006:**

Nakamura H, Arakawa K, Itakura H, Kitabatake A, Goto Y, Toyota T, Nakaya N, Nishimoto S, Muranaka M, Yamamoto A, Mizuno K, Ohashi Y Primary prevention of cardiovascular disease with pravastatin in Japan (MEGA Study): a prospective randomised controlled trial. Lancet 2006 Sep 30;368:1155-63 [17011942]

Nakamura H [Primary prevention trial by lowering hyperlipidemia on the cardiovascular disease (MEGA Study)] Nippon Ronen Igakkai Zasshi 2009;46:18-21 [19246826]

**Milner, 1989:**

Milner MR, Gallino RA, Leffingwell A, Pichard AD, Brooks-Robinson S, Rosenberg J, Little T, Lindsay J Jr Usefulness of fish oil supplements in preventing clinical evidence of restenosis after percutaneous transluminal coronary angioplasty. Am J Cardiol 1989 Aug 1;64:294-9 [2526993]

**Hong, 2005:**

Hong YJ, Jeong MH, Hyun DW, Hur SH, Kim KB, Kim W, Lim SY, Lee SH, Hong SN, Kang DG, Yun KH, Kim KH, Lee YS, Park HW, Kim JH, Ahn YK, Cho JG, Park JC, Kang JC Prognostic significance of simvastatin therapy in patients with ischemic heart failure who underwent percutaneous coronary intervention for acute myocardial infarction. Am J Cardiol 2005;95:619-22 [15721103]

**GISSI, 1999:**

Dietary supplementation with n-3 polyunsaturated fatty acids and vitamin E after myocardial infarction: results of the GISSI-Prevenzione trial. Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto miocardico. Lancet 1999 Aug 7;354:447-55 [10465168]

**PPP, 2001:**

de Gaetano G Low-dose aspirin and vitamin E in people at cardiovascular risk: a randomised trial in general practice. Collaborative Group of the Primary Prevention Project. Lancet 2001 Jan 13;357:89-95 [11197445]

**FATS, 1990:**

Brown G, Albers JJ, Fisher LD, Schaefer SM, Lin JT, Kaplan C, Zhao XQ, Bisson BD, Fitzpatrick VF, Dodge HT Regression of coronary artery disease as a result of intensive lipid-lowering therapy in men with high levels of apolipoprotein B. N Engl J Med 1990 Nov 8;323:1289-98 [2215615]

**ODYSSEY OPTIONS I, :**

Robinson JG, Colhoun HM, Bays HE, Jones PH, Du Y, Hanotin C, Donahue S Efficacy and safety of alirocumab as add-on therapy in high-cardiovascular-risk patients with hypercholesterolemia not adequately controlled with atorvastatin (20 or 40 mg) or rosuvastatin (10 or 20 mg): design and rationale of the ODYSSEY OPTIONS Studies. Clin Cardiol 2014 Oct;37:597-604 [25269777]

Bays H, Gaudet D, Weiss R, Ruiz JL, Watts GF, Gouni-Berthold I, Robinson J, Zhao J, Hanotin C, Donahue S Alirocumab as Add-on To Atorvastatin Versus Other Lipid Treatment Strategies: ODYSSEY OPTIONS I Randomized Trial. J Clin Endocrinol Metab 2015 Jun 1;:jc20151520 [26030325]

**ODYSSEY OPTIONS II, :**

Robinson JG, Colhoun HM, Bays HE, Jones PH, Du Y, Hanotin C, Donahue S Efficacy and safety of alirocumab as add-on therapy in high-cardiovascular-risk patients with hypercholesterolemia not adequately controlled with atorvastatin (20 or 40 mg) or rosuvastatin (10 or 20 mg): design and rationale of the ODYSSEY OPTIONS Studies. Clin Cardiol 2014 Oct;37:597-604 [25269777]

**ODYSSEY MONO, :**

Roth EM, Taskinen MR, Ginsberg HN, Kastelein JJ, Colhoun HM, Robinson JG, Merlet L, Pordy R, Baccara-Dinet MT Monotherapy with the PCSK9 inhibitor alirocumab versus ezetimibe in patients with hypercholesterolemia: results of a 24 week, double-blind, randomized Phase 3 trial. Int J Cardiol 2014;176:55-61 [25037695]

## **GAUSS 2, :**

Stroes E, Colquhoun D, Sullivan D, Civeira F, Rosenson RS, Watts GF, Bruckert E, Cho L, Dent R, Knusel B, Xue A, Scott R, Wasserman SM, Rocco M Anti-PCSK9 antibody effectively lowers cholesterol in patients with statin intolerance: the GAUSS-2 randomized, placebo-controlled phase 3 clinical trial of evolocumab. *J Am Coll Cardiol* 2014 Jun 17;63:2541-8 [[24694531](#)]

## **MacMillan, 1960:**

MACMILLAN RL, BROWN K, WATT DL Long-term anticoagulant therapy after myocardial infarction. *Can Med Assoc J* 1960;83:567-70 [[14419608](#)]

MACMILLAN RL, BROWN K, WATT DL Long-term anticoagulant therapy after myocardial infarction. *Can Med Assoc J* 1960;83:567-70 [[14419608](#)]

## **Borchegrevink, 1960:**

## **Clausen, 1961:**

CLAUSEN J, ANDERSEN PE, ANDRESEN P, GRUELUND S, HARSLOF E, ANDERSEN UH, JORGENSEN J, MOSE C [Long-term anticoagulant treatment after acute coronary occlusion. Material with complete comparison with control material]. *Ugeskr Laeger* 1961;123:987-94 [[13693953](#)]

## **Harvald, 1961:**

## **Conrad, 1964:**

CONRAD LL, KYRIACOPOULOS JD, WIGGINS CW, HONICK GL PREVENTION OF RECURRENCES OF MYOCARDIAL INFARCTION; A DOUBLE-BLIND STUDY OF THE EFFECTIVENESS OF LONG-TERM ORAL ANTICOAGULANT THERAPY. *Arch Intern Med* 1964;114:348-58 [[14171625](#)]

## **Wasserman, 1966:**

Wasserman AJ, Gutterman LA, Yoe KB, Kemp VE Jr, Richardson DW Anticoagulants in acute myocardial infarction. The failure of anticoagulants to alter mortality in a randomized series. *Am Heart J* 1966;71:43-9 [[5900864](#)]

## **Loeliger, 1967:**

Loeliger EA, Hensen A, Kroes F, van Dijk LM, Fekkes N, de Jonge H, Hemker HC A double-blind trial of long-term anticoagulant treatment after myocardial infarction. *Acta Med Scand* 1967;182:549-66 [[4862156](#)]

## **Lovell, 1967:**

## **Seaman, 1969:**

Seaman AJ, Griswold HE, Reaume RB, Ritzmann L Long-term anticoagulant prophylaxis after myocardial infarction. *N Engl J Med* 1969;281:115-9 [[4307139](#)]  
[10.1056/NEJM196907172810301](#)

## **Sorensen, 1969:**

Sorensen OH, Friis T, Jorgensen AW, Jorgensen MB, Nissen NI Anticoagulant treatment of acute coronary thrombosis. *Acta Med Scand* 1969;185:65-72 [[4185116](#)]

## **Meuwisse,, 1969:**

Meuwissen OJ, Vervoorn AC, Cohen O, Jordan FL, Nelemans FA Double blind trial of long-term anticoagulant treatment after myocardial infarction. *Acta Med Scand* 1969;186:361-8 [[4985108](#)]

## **Drapkin and Merskey, 1972:**

Drapkin A, Merskey C Anticoagulant therapy after acute myocardial infarction. Relation of therapeutic benefit to patient's age, sex, and severity of infarction. *JAMA* 1972;222:541-8 [[4117261](#)]

## **Apenstrom and Korsan-Bengtzen, 1964:**

ASPENSTROEM G, KORSAN-BENGTSEN K A DOUBLE BLIND STUDY OF DICUMAROL PROPHYLAXIS IN CORONARY HEART DISEASE. *Acta Med Scand* 1964;176:563-75 [[14223532](#)]

## **Sakamoto, 2006:**

Sakamoto T, Kojima S, Ogawa H, Shimomura H, Kimura K, Ogata Y, Sakaino N, Kitagawa A Effects of early statin treatment on symptomatic heart failure and ischemic events after acute myocardial infarction in Japanese. *Am J Cardiol* 2006;97:1165-71 [[16616020](#)] [10.1016/j.amjcard.2005.11.031](#)

## **5 stable angina**



<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>dactinomycin eluting stent vs bare-metal stent</b>			
<b>ACTION , 2004</b> n=241/119 follow-up: 6 months	Multilink Tetra stent versus uncoated Multilink Tetra stent	Patients with stable angina pectoris orsilent ischemia and a single de novo lesion in a nativecoronary artery $\geq 3.0$ mm and $\leq 4.0$ mm in diameter thatcould be covered by an 18-mm stent	Parallel groups single-blind worldwide
<b>paclitaxel eluting stent vs bare-metal stent</b>			
<b>SCORE , 2004</b> n=126/140 follow-up: 12 months	QuaDDS stents (paclitaxel) versus uncoated control stents	patients with focal, de novo coronary lesions	Parallel groups open Worldwide
<b>TAXUS I , 2003</b> n=31/30 follow-up: 12 months	TAXUS NIR versus NIR stent	Stable or unstable AP, silent ischaemia; single de novo or restenotic coronary lesions	Parallel groups double-blind Germany
<b>TAXUS II , 2003</b> [NCT00299026] n=266/270 follow-up: 12 months	TAXUS versus NIR stent	Stable or unstable AP, silent ischaemia; single de novo target lesion with estimatedstenosis $>50\%$ and $<99\%$ ,	Parallel groups double-blind Global
<b>TAXUS IV , 2004</b> [NCT00292474] n=662/652 follow-up: 9 months	TAXUS versus EXPRESS	Stable or unstable AP, provokable ischaemia with a single, previously untreated coronary-artery stenosis (vessel diameter, 2.5 to 3.75 mm; lesion length, 10 to 28 mm)	Parallel groups double-blind United States
<b>TAXUS V (all patients) , 2005</b> [NCT00301522] n=577/579 follow-up: 9 months	TAXUS versus bare metal EXPRESS-2	Stable or unstable AP, silent ischaemia with single coronary artery stenosis including complex or previously unstudied lesions (requiring 2.25-mm, 4.0-mm, and/or multiple stents)	Parallel groups double-blind United States
<b>TAXUS VI , 2005</b> [NCT00297804] n=219/227 follow-up: 9 months (2y)	TAXUS versus Express2 stent	Stable or unstable AP, silent ischaemia with long, complex coronary artery lesions	Parallel groups double-blind Europe
<b>BASKET-SAVAGE</b> <i>ongoing</i> [NCT00595647] n=NA follow-up:	Taxus versus Libert	percutaneous coronary interventions of saphenous vein grafts	open
<b>paclitaxel, non-polymeric eluting stent vs bare-metal stent</b>			
<b>ASPECT , 2003</b> [NCT00196079] n=117/58 follow-up: 6 months	coated Supra-G stent versus Supra-G stent	patientswith discrete coronary lesions ( $<15$ mm in length, 2.25 to 3.5 mm in diameter)	Parallel groups double-blind

continued...



<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>DELIVER , 2004</b> n=524/519 follow-up: 9 months	non-polymer-based paclitaxel-coated ACHIEVE stent versus stainless steel Multi-Link (ML) PENTA stent	patients with focal de novo coronary lesions, <25 mm in length, in 2.5- to 4.0-mm vessels	Parallel groups single-blind US
<b>ELUTES , 2004</b> n=152/38 follow-up: 12 months	coated V-Flex Plus versus V-Flex Plus	single de novo type A or type B1 lesions 15 mm length in a nativecoronary artery	Parallel groups open Europe
<b>PATENCY , 2002</b> <i>unpublished</i> n=24/26 follow-up: 9 months	Logic PTX paclitaxel Eluting CoronaryStents versus uncoated control stents	Patients with de novo lesions of 2.7- to 4.0-mm diameter and 25-mm length received 3.0, 3.5, or 4.0 mm 10- or 15-mm	Parallel groups double blind
<b>zotarolimus eluting stent vs bare-metal stent</b>			
<b>ENDEAVOR II , 2006</b> n=598/599 follow-up: 12 months	AVE Zotarolimus-Eluting Driver versus Driver	single de novo native coronary artery stenosis	Parallel groups double-blind worldwide
<b>TMR+CABG vs CABG</b>			
<b>Allen , 2000</b> n=132/131 follow-up:	coronary bypass of suitable vessels plus transmyocardial revascularization to areas not graftable versus coronary bypass alone with nongraftable areas left unvascularized	patients whose standard of care was coronary artery bypass grafting and who had one or more ischemic areas not amenable to bypass grafting	single blind
<b>Loubani , 2003</b> n=10/10 follow-up: 36 months	coronary artery bypass grafting plus transmyocardial laser revascularization with a holmium:YAG (yttrium-aluminum-garnet) laser to nongraftable areas versus coronary artery bypass grafting	Patients who had elective coronary artery bypass with one or more nongraftable coronary arteries	Parallel groups open UK
<b>Zhao , 2006</b> n=40/40 follow-up: 3.4y	transmyocardial laser revascularization (holmium: YAG) combined with off-pump coronary artery bypass versus off-pump coronary artery bypass	patients with diffusely diseased target vessels	Parallel groups open China
<b>dipyridamol vs control</b>			
<b>Atlanta (Sbar) , 1967</b> n=30/30 follow-up: 6 months	dipyridamole 150mg daily versus placebo	patients with angina pectoris	parallel groups double-blind

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>Wirecki , 1967</b> n=28/28 follow-up: 7 months	dipyridamole 150mg daily versus placebo	patients with angina pectoris	parallel groups double blind
<b>Becker , 1967</b> n=14/13 follow-up: 5 months	dipyridamole 225mg daily versus placebo	-	parallel groups double-blind
<b>bioabsorbable polymer EES vs everolimus eluting stent</b>			
<b>EVOLVE , 2012</b> [NCT01135225] n=NA follow-up: 30 days	bioabsorbable polymer everolimus-eluting stent versus polymer EES	patients with a de novo lesion 28 mm in length, in a coronary artery of 2.25 to 3.5 mm diameter	Parallel groups single blind
<b>balloon angioplasty vs medical treatment</b>			
<b>RITA 2 , 1997</b> n=504/514 follow-up: 7y	PTCA within 3 mo of the randomisation versus medical treatment	Angina leading to admission within 90days, previous Q wave MI, no previousPTCA, no left main stem disease	Parallel groups open UK
<b>ACME , 1992</b> n=105/107 follow-up: 5y	PTCA within 3 days of randomization versus medical treatment (nitrates, beta-blockers, calcium blockers)	Stable angina, history of angina, MIwithin 3 months, exercise test with STdepression >3 mm, no previous PTCA; Single or serial stenosis within sameartery 70% to 99% proximal twothirds	Parallel groups open US
<b>ACME 2 (Folland) , 1997</b> n=51/50 follow-up: 5y	PTCA versus medical therapy	Stable angina, history of angina, MIwithin 3 months, exercise test with STdepression >3 mm, no previous PTCA; Stenosis >70% proximal two thirds,no main artery stenosis >50% , no 3vessel disease	Parallel groups open
<b>ACIP , 1997</b> n=192/366 follow-up: 24 months	revascularization by angioplasty or bypass surgery versus angina-guided drug therapy or angina plus ischemia-guided drug therapy	clinically stable patients with angiographically documented coronary disease (50% stenosis in 1 major vessel or branch) suitable for revascularization	Parallel groups open
<b>INSPIRE , 2006</b> n=104/101 follow-up: 60 months	coronary revascularization for suppressing scintigraphic ischemia versus intensive medical therapy strategy	Stable survivors of MI, total perfusion defect size 20% , ischemic defect size 10% (by adenosine SPECT), EF 35% t	Parallel groups open
<b>SWISSI II , 2007</b> [NCT00387231] n=96/105 follow-up: 10.2y	Percutaneous coronary intervention aimed at full revascularization versus intensive anti-ischemic drug therapy	patients with a recent MI, silent myocardial ischemia verified by stress imaging, and 1- or 2-vessel coronary artery disease	Parallel groups open Switzerland

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>MASS , 1995</b> n=72/72 follow-up: 5y	PTCA versus medical treatment (aspirin, nitrates, beta-blockers and calcium channel blocking	Stable angina, no Q wave MI, no leftventricular dysfunction	Parallel groups open Brazil
<b>Sievers , 1993</b> n=44/44 follow-up: 2y	PTCA versus medical treatment	Previous nonQ wave MI, no angina indaily life, no previous Q wave MI	Parallel groups open Germany
<b>spinal cord stimulation vs no spinal cord stimulation</b>			
<b>de Jongste , 1994</b> n=8/9 follow-up: 8 weeks	spinal cord stimulation versus control	patients with intractable angina pectoris	Parallel groups open
<b>Lanza , 2005</b> n=10/10 follow-up: 8 mo (median)	spinal cord stimulation versus no spinal cord stimulation	patients with cardiac syndrome X	Cross over open
<b>aspirin vs placebo</b>			
<b>SAPAT , 1992</b> n=1009/1026 follow-up: 50 months	aspirin 75 mg daily versus placebo	patients with stable chronic angina pectoris	Parallel groups double blind Sweden
<b>Azithromycin vs placebo</b>			
<b>Gupta et al , 1997</b> n=43/41 follow-up: 65279;18mo	65279;Azithromycin 500 mg/d for 3 d (28 received 1 course, 12 received 2 courses 3 mo apart) versus placebo	Male patients at least 6 mo from documented MI and with titers to Chlamydia pneumoniae $\geq 1:64$	Parallel groups double blind
<b>ACADEMIC , 1999</b> n=150/152 follow-up: 2y	Azithromycin 500 mg/d for 3 d then 500 mg/wk for 3 mo versus placebo	Patients with CAD and C pneumoniae titers of $\geq 1:16$ . Patients were at least 5 d from an MI	Parallel groups double blind
<b>STAMINA (Azithromycin) , 2002</b> n=111/107 follow-up: 1y	Azithromycin 500 mg/d for 3 d plus omeprazole 20 mg 2/d for 1 wk plus metronidazole 400 mg 2/d for 1 wk versus placebo	Patients with ACS	Parallel groups double blind England
<b>AZACS , 2003</b> n=2004/2008 follow-up: 6mo	Azithromycin 500 mg on day 1 followed by 250 mg/d for 4d versus placebo	Patients with ACS	Parallel groups double blind

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>WIZARD , 2003</b> n=3879/3868 follow-up: 14mo	Azithromycin 600 mg/d for 3 d then 1/wk for 11 wk versus placebo	Patients with a history of MI of more than 6 weeks before and with C pneumoniae titers of >=1:16	Parallel groups double blind North America, Europe, Argentina, India
<b>ACES , 2005</b> [NCT00000617] n=2004/2008 follow-up: 4y	Azithromycin 600 mg/wk for 1 y versus placebo	Patients with stable CAD	Parallel groups double blind US
<b>clarithromycin vs placebo</b>			
<b>CLARIFY , 2001</b> n=74/74 follow-up: 1y	Clarithromycin 500 mg/d for 85 d versus placebo	Patients with ACS	Parallel groups double blind
<b>CLARICOR , 2006</b> [NCT00121550] n=2172/2201 follow-up: 3 years	clarithromycin 500 mg/day versus placebo	patients with a discharge diagnosis of myocardial infarction or angina pectoris	Parallel groups double blind Denmark
<b>dipyridamol vs placebo</b>			
<b>Kinsella , 1962</b> n=13/13 follow-up: 0.5 months	dipyridamole 37.5 mg and 100mg daily versus placebo	-	parallel groups double-blind
<b>Leiberman , 1964</b> n=19/19 follow-up: >3 months	dipyridamole 100mg daily versus placebo	-	parallel groups double blind
<b>Zion , 1961</b> n=14/14 follow-up: 0.5 months	Dipyridamole 37.5mg versus placebo	patients with angina pectoris	cross-over double-blind
<b>Dewar , 1961</b> n=17/17 follow-up: 0.5 months	Dipyridamole 100mg daily versus placebo	patients with angina pectoris	parallel groups double-blind
<b>Neumann , 1964</b> n=20/16 follow-up: 1.5 months	dipyridamole 150mg daily versus placebo	elderly with precordial pain	parallel groups double-blind
<b>Foulds , 1960</b> n=24/24 follow-up: 1 months	Dipyridamole 200mg daily versus placebo	patients with angina pectoris	parallel groups double-blind
<b>Igloe , 1970</b> n=26/22 follow-up: 2-7 months	Dipyridamole 200mg daily versus placebo	patients with angina pectoris	parallel groups double blind
<b>Gatifloxacin vs placebo</b>			
<b>PROVE-IT , 2005</b> n=2076/2086 follow-up: 24mo	Gatifloxacin 400 mg/d for 10 d/mo for 2y versus placebo	Patients hospitalized with ACS in the preceding 10 d	Parallel groups double blind
<b>ivabradine 10mg vs placebo</b>			

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>Borer (CL2-009) 10mg , 2003</b> n=91/91 follow-up: 2 weeks	Ivabradine 5 mg twice daily (10mg/d) versus placebo		double blind
<b>ivabradine 15mg vs placebo</b>			
<b>BEAUTIFUL , 2008</b> [NCT00143507] n=5479/5438 follow-up: 19 months (range 16-24)	ivabradine target dose of 75 mg twice a day versus placebo	patients with coronary artery disease and left-ventricular systolic dysfunction (LVEF <=40% )	double blind 33 countries
<b>ivabradine 20mg vs placebo</b>			
<b>SIGNIFY , 2014</b> [ISRCTN61576291] n=9550/9552 follow-up: 27.8 mo (median)	ivabradine, at a dose of up to 10 mg twice daily, with the dose adjusted to achieve a target heart rate of 55 to 60 beats per minute. versus placebo	patients who had both stable coronary artery disease without clinical heart failure and a heart rate of 70 beats per minute or more	Parallel groups double-blind
<b>Borer (CL2-009) 20mg , 2003</b> n=88/91 follow-up: 2 weeks	ivabradine 10mg twice daily (20mg/d) versus placebo		double blind
<b>ivabradine 5mg vs placebo</b>			
<b>Borer (CL2-009) 5mg , 2003</b>  n=90/91 follow-up: 2 weeks	-	-	Parallel groups double blind
<b>ranolazine 1000mg vs placebo</b>			
<b>MARIZA , 2004</b> n=191/191 follow-up: 1 week	ranolazine 500 mg twice daily (sustained-release ranolazine 500, 1,000, or 1,500 mg) versus placebo	Patients with angina-limited exercise	Cross over double blind US, Czech Republic, Poland, Canada
<b>RAN080 , 2005</b> n=158/158 follow-up: 1 week	ranolazine IR 400mg TID versus placebo	patients who had symptom-limited exercise	Cross over double blind Europe, canada
<b>roxifiban vs placebo</b>			
<b>Murphy , 2003</b> n=120 follow-up: 30 days	roxifiban 0.25, 0.5, 0.75, 1, 1.25, 1.5, 2, or 2.5 mg/day for up to 30 days versus placebo	patients with stable coronary artery disease	Parallel groups double blind
<b>spinal cord stimulation vs placebo</b>			

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>Eddicks , 2007</b> n=12/12 follow-up: 4 weeks	Spinal cord stimulation versus placebo	patients with refractory angina	Cross over double blind
<b>ivabradine 15mg vs placebo (on top standard treatment)</b>			
<b>BEAUTIFUL (angina subgroup)</b> n=734/773 follow-up: 19 months (range 16-24)	ivabradine target dose of 75 mg twice a day versus placebo	patients with stable coronary artery disease and left ventricular systolic dysfunction with limiting angina	double blind 33 countries
<b>ranolazine 1000mg vs placebo (on top standard treatment)</b>			
<b>CARISA 1000mg , 2004</b> n=261/258 follow-up: 12 weeks	ranolazine 1000mg (in combination with beta-blockers or calcium antagonists) versus placebo	patients with severe chronic angina who have symptoms of chronic angina and who experience angina and ischemia at low workloads despite taking standard doses of atenolol, amlodipine, or diltiazem	Parallel groups double blind
<b>ranolazine 1000mg + amlodipine vs placebo + amlodipine</b>			
<b>ERICA , 2006</b> [NCT00091429] n=281/284 follow-up: 6 weeks	ranolazine 1000 mg twice a day for 6 weeks + amlodipine (10 mg/d) versus placebo + amlodipine (10 mg/d)	patients with stable chronic angina already treated with the maximal dose of amlodipine (10mg/d)	Parallel groups double blind Europe, USA, Canada
<b>ivabradine 10mg vs placebo on top of amlodipine</b>			
<b>CL3-018 10mg , 3000</b> <i>unpublished</i> n=232/252 follow-up: 12 weeks	ivabradine 5mg twice daily (10mg/d) versus placebo	-	Parallel groups
<b>ivabradine 15mg vs placebo on top of amlodipine</b>			
<b>CL3-018 15mg , 3000</b> <i>unpublished</i> n=244/252	ivabradine 7.5mg twice daily (15mg/d) versus placebo	-	
<b>ivabradine 15mg vs placebo on top of atenolol</b>			
<b>ASSOCIATE (Tardif) , 2009</b> [NCT00202566] n=449/440 follow-up: 4 months	ivabradine 5 mg b.i.d. for 2 months, increased to 7.5 mg b.i.d. for a further 2 months (on top atenolol 50 mg/day ) versus placebo on top atenolol 50 mg/day	patients with stable angina receiving atenolol 50 mg/day or another beta-blocker at equivalent doses for at least 3 months	Parallel groups double blind 20 countries
<b>A vs B</b>			
<b>Nordic Bifurcation Study</b> <i>ongoing</i> [NCT00376571] n=NA follow-up:	Strategy of Routine Stenting Both Main Vessel and Side Branch versus Strategy of Routine Main Vessel Stenting and Optional Treatment of Side Branch	bifurcation lesions	
<b>dexamethasone eluting stent vs bare-metal stent</b>			

continued...

Trial	Treatments	Patients	Trials design and methods
FEMH-93005 <i>ongoing</i> [NCT00190099] n=NA	-	-	
<b>ivabradine vs amlodipine</b>			
CL3-023 (15mg) <i>unpublished</i> n=381/398 follow-up: 3 months	ivabradine 7.5mg twice daily versus amlodipine		Parallel groups double-blind
CL3-023 (20mg) <i>unpublished</i> n=376/398 follow-up: 3 months	ivabradine 10mg twice daily versus amlodipine		double-blind

More details and results :

- myocardial revascularization for stable angina in all type of patient at <http://www.trialresultscenter.org/go-Q25>
- myocardial revascularization for stable angina in single vessel disease at <http://www.trialresultscenter.org/go-Q27>
- myocardial revascularization for stable angina in multivessels disease at <http://www.trialresultscenter.org/go-Q28>
- myocardial revascularization for stable angina in diabetic patients at <http://www.trialresultscenter.org/go-Q29>
- antithrombotics for stable angina in all type of patient at <http://www.trialresultscenter.org/go-Q33>
- antibiotics for stable angina in all type of patient at <http://www.trialresultscenter.org/go-Q34>
- HR-slowng agents for stable angina in patients with left ventricular dysfunction at <http://www.trialresultscenter.org/go-Q118>
- HR-slowng agents for stable angina in all type of patients at <http://www.trialresultscenter.org/go-Q262>
- anti-anginal drugs for stable angina in all type of patients at <http://www.trialresultscenter.org/go-Q263>
- spinal cord stimulation for stable angina in patients with severe/refractory angina pectoris at <http://www.trialresultscenter.org/go-Q358>
- myocardial revascularization for stable angina in patients with Left Ventricular Dysfunction at <http://www.trialresultscenter.org/go-Q501>

## References

### **ACTION, 2004:**

Serruys PW, Veldhof S, Stuteville M, et al Actinomycin-elutingstent improves outcome by reducing neointimal hyperplasia Transcatheter Cardiovascular Therapeutics Annual Meeting, September, 2002

Serruys PW, Ormiston JA, Sianos G, Sousa JE, Grube E, den Heijer P, de Feyter P, Buszman P, Schmig A, Marco J, Polonski L, Thuesen L, Zeiher AM, Bett JH, Suttorp MJ, Glogar HD, Pitney M, Wilkins GT, Whitbourn R, Veldhof S, Miquel K, Johnson R, Coleman L, Actinomycin-eluting stent for coronary revascularization: a randomized feasibility and safety study: the ACTION trial. J Am Coll Cardiol 2004 Oct 6;44:1363-7 [15464314]

### **SCORE, 2004:**

Stone GW. Adverse outcomes from a taxane-loaded polymeric sleeve stent: final results from the SCORE Trial American College of Cardiology Scientific Session, March, 2002

Grube E, Lansky A, Hauptmann KE, Di Mario C, Di Sciascio G, Colombo A, Silber S, Stumpf J, Reifart N, Fajadet J, Marzocchi A, Schofer J, Dumas P, Hoffmann R, Guagliumi G, Pitney M, Russell ME High-dose 7-hexanoyltaxol-eluting stent with polymer sleeves for coronary revascularization: one-year results from the SCORE randomized trial. J Am Coll Cardiol 2004 Oct 6;44:1368-72 [15464315]

**TAXUS I, 2003:**

Grube E, Silber S, Hauptmann KE, Mueller R, Buellesfeld L, Gerckens U, Russell ME TAXUS I: six- and twelve-month results from a randomized, double-blind trial on a slow-release paclitaxel-eluting stent for de novo coronary lesions. *Circulation* 2003;107:38-42 [[12515740](#)]

Grube E, Silber S, Hauptmann KE, Mueller R, Buellesfeld L, Gerckens U, Russell ME TAXUS I: six- and twelve-month results from a randomized, double-blind trial on a slow-release paclitaxel-eluting stent for de novo coronary lesions. *Circulation* 2003 Jan 7;107:38-42 [[12515740](#)]

**TAXUS II, 2003:**

Colombo A, Drzewiecki J, Banning A, Grube E, Hauptmann K, Silber S, Dudek D, Fort S, Schiele F, Zmudka K, Guagliumi G, Russell ME Randomized study to assess the effectiveness of slow- and moderate-release polymer-based paclitaxel-eluting stents for coronary artery lesions. *Circulation* 2003;108:788-94 [[12900339](#)]

Silber S, Colombo A, Banning AP, Hauptmann K, Drzewiecki J, Grube E, Dudek D, Baim DS Final 5-year results of the TAXUS II trial: a randomized study to assess the effectiveness of slow- and moderate-release polymer-based paclitaxel-eluting stents for de novo coronary artery lesions. *Circulation* 2009 Oct 13;120:1498-504 [[19786634](#)]

**TAXUS IV, 2004:**

Stone GW, Ellis SG, Cox DA, Hermiller J, O'Shaughnessy C, Mann JT, Turco M, Caputo R, Bergin P, Greenberg J, Popma JJ, Russell ME A polymer-based, paclitaxel-eluting stent in patients with coronary artery disease. *N Engl J Med* 2004;350:221-31 [[14724301](#)]

Ellis SG, Stone GW, Cox DA, Hermiller J, O'Shaughnessy C, Mann T, Turco M, Caputo R, Bergin PJ, Bowman TS, Baim DS Long-Term Safety and Efficacy With Paclitaxel-Eluting Stents 5-Year Final Results of the TAXUS IV Clinical Trial (TAXUS IV-SR: Treatment of De Novo Coronary Disease Using a Single Paclitaxel-Eluting Stent). *JACC Cardiovasc Interv* 2009 Dec;2:1248-59 [[20129552](#)] [10.1016/j.jcin.2009.10.003](#)

Ellis SG, Stone GW, Cox DA, Hermiller J, O'Shaughnessy C, Mann T, Turco M, Caputo R, Bergin PJ, Bowman TS, Baim DS Long-term safety and efficacy with paclitaxel-eluting stents: 5-year final results of the TAXUS IV clinical trial (TAXUS IV-SR: Treatment of De Novo Coronary Disease Using a Single Paclitaxel-Eluting Stent). *JACC Cardiovasc Interv* 2009;2:1248-59 [[20129552](#)] [10.1016/j.jcin.2009.10.003](#)

**TAXUS V (all patients), 2005:**

Stone GW, Ellis SG, Cannon L, Mann JT, Greenberg JD, Spriggs D, O'Shaughnessy CD, DeMaio S, Hall P, Popma JJ, Koglin J, Russell ME Comparison of a polymer-based paclitaxel-eluting stent with a bare metal stent in patients with complex coronary artery disease: a randomized controlled trial. *JAMA* 2005;294:1215-23 [[16160130](#)]

**TAXUS VI, 2005:**

Dawkins KD, Grube E, Guagliumi G, Banning AP, Zmudka K, Colombo A, Thuesen L, Hauptman K, Marco J, Wijns W, Popma JJ, Koglin J, Russell ME Clinical efficacy of polymer-based paclitaxel-eluting stents in the treatment of complex, long coronary artery lesions from a multicenter, randomized trial: support for the use of drug-eluting stents in contemporary clinical practice. *Circulation* 2005;112:3306-13 [[16286586](#)]

Grube E, Dawkins KD, Guagliumi G, Banning AP, Zmudka K, Colombo A, Thuesen L, Hauptman K, Marco J, Wijns W, Popma JJ, Buellesfeld L, Koglin J, Russell ME TAXUS VI 2-year follow-up: randomized comparison of polymer-based paclitaxel-eluting with bare metal stents for treatment of long, complex lesions. *Eur Heart J* 2007;28:2578-82 [[17938126](#)]

Grube E, Dawkins K, Guagliumi G, Banning A, Zmudka K, Colombo A, Thuesen L, Hauptman K, Marco J, Wijns W, Joshi A, Mascioli S TAXUS VI final 5-year results: a multicentre, randomised trial comparing polymer-based moderate-release paclitaxel-eluting stent with a bare metal stent for treatment of long, complex coronary artery lesions. *EuroIntervention* 2009;4:572-7 [[19378676](#)]

**BASKET-SAVAGE, 0:**

ongoing trial NCT00595647

**ASPECT, 2003:**

Park SJ, Shim WH, Ho DS, Raizner AE, Park SW, Hong MK, Lee CW, Choi D, Jang Y, Lam R, Weissman NJ, Mintz GS A paclitaxel-eluting stent for the prevention of coronary restenosis. *N Engl J Med* 2003;348:1537-45 [[12700373](#)]

**DELIVER, 2004:**

O'Neill WW, Knopf W, Lansky A, Fitzgerald P, Mahaffey K. Randomized comparison of paclitaxel-coated versus metallic stents for treatment of coronary lesions American College of Cardiology Scientific Session, March, 2003

Knopf W, O'Neill WW, Lansky A, Fitzgerald P, Mahaffey KE Randomized comparison of paclitaxel-coated versus metallic stents for treatment of coronary lesions Transcatheter Cardiovascular Therapeutics Annual Meeting, September, 2003



Lansky AJ, Costa RA, Mintz GS, Tsuchiya Y, Midei M, Cox DA, O'Shaughnessy C, Applegate RA, Cannon LA, Mooney M, Farah A, Tannenbaum MA, Yakubov S, Kereiakes DJ, Wong SC, Kaplan B, Cristea E, Stone GW, Leon MB, Knopf WD, O'Neill WW Non-polymer-based paclitaxel-coated coronary stents for the treatment of patients with de novo coronary lesions: angiographic follow-up of the DELIVER clinical trial. *Circulation* 2004 Apr 27;109:1948-54 [[15078794](#)]

**ELUTES, 2004:**

Gershlick A, De Scheerder I, Chevalier B, Stephens-Lloyd A, Camenzind E, Vrints C, Reifart N, Missault L, Goy JJ, Brinker JA, Raizner AE, Urban P, Heldman AW Inhibition of restenosis with a paclitaxel-eluting, polymer-free coronary stent: the European evaluation of paclitaxel eluting stent (ELUTES) trial. *Circulation* 2004;109:487-93 [[14744971](#)]

**PATENCY, 2002:**

unpublished

Heldman A, Farhat N, Fry E, et al. Paclitaxel-eluting stent for cytostatic prevention of restenosis: the PATENCY Study Transcatheter Cardiovascular Therapeutics Annual Meeting, September, 2002

**ENDEAVOR II, 2006:**

Gruberg L. ENDEAVOR II. A randomized comparison of the Endeavor ABT-578 drug-eluting stent with a bare metal stent for coronary revascularization, <http://www.medscape.com/viewarticle/501475>

Fajadet J, Wijns W, Laarman GJ, Kuck KH, Ormiston J, Mnzl T, Popma JJ, Fitzgerald PJ, Bonan R, Kuntz RE Randomized, double-blind, multicenter study of the Endeavor zotarolimus-eluting phosphorylcholine-encapsulated stent for treatment of native coronary artery lesions: clinical and angiographic results of the ENDEAVOR II trial. *Circulation* 2006 Aug 22;114:798-806 [[16908773](#)]

Fajadet J, Wijns W, Laarman GJ, Kuck KH, Ormiston J, Mnzl T, Popma JJ, Fitzgerald PJ, Bonan R, Kuntz RE Randomized, double-blind, multicenter study of the Endeavor zotarolimus-eluting phosphorylcholine-encapsulated stent for treatment of native coronary artery lesions. Clinical and angiographic results of the ENDEAVOR II Trial. *Minerva Cardioangiol* 2007 Feb;55:1-18 [[17287679](#)]

Sakurai R, Hongo Y, Yamasaki M, Honda Y, Bonneau HN, Yock PG, Cutlip D, Popma JJ, Zimetbaum P, Fajadet J, Kuntz RE, Wijns W, Fitzgerald PJ Detailed intravascular ultrasound analysis of Zotarolimus-eluting phosphorylcholine-coated cobalt-chromium alloy stent in de novo coronary lesions (results from the ENDEAVOR II trial). *Am J Cardiol* 2007 Sep 1;100:818-23 [[17719326](#)]

Eisenstein EL, Wijns W, Fajadet J, Mauri L, Edwards R, Cowper PA, Kong DF, Anstrom KJ Long-Term Clinical and Economic Analysis of the Endeavor Drug-Eluting Stent Versus the Driver Bare-Metal Stent 4-Year Results From the ENDEAVOR II Trial (Randomized Controlled Trial to Evaluate the Safety and Efficacy of the Medtronic AVE ABT-578 Eluting Driver Coronary Stent in De Novo Native Coronary Artery Lesions). *JACC Cardiovasc Interv* 2009 Dec;2:1178-87 [[20129543](#)]  
[10.1016/j.jcin.2009.10.011](#)

**Allen, 2000:**

Allen KB, Dowling RD, DelRossi AJ, Realyvasques F, Lefrak EA, Pfeffer TA, Fudge TL, Mostovych M, Schuch D, Szentpetery S, Shaar CJ Transmyocardial laser revascularization combined with coronary artery bypass grafting: a multicenter, blinded, prospective, randomized, controlled trial. *J Thorac Cardiovasc Surg* 2000;119:540-9 [[10694615](#)]

**Loubani, 2003:**

Loubani M, Chin D, Leverment JN, Galianes M Mid-term results of combined transmyocardial laser revascularization and coronary artery bypass. *Ann Thorac Surg* 2003;76:1163-6 [[14530005](#)]

**Zhao, 2006:**

Zhao H, Wan F, Guo JX, Chen Y, Xie JY, Yang W, Zhang P [Chronic effects of transmyocardial laser revascularization combined with off-pump coronary artery bypass (OPCAB) compared with OPCAB alone in patients with ischemic heart disease: a prospective multicenter follow-up study] *Zhonghua Xin Xue Guan Bing Za Zhi* 2006;34:710-3 [[17081396](#)]

**Atlanta (Sbar), 1967:**

Sbar S, Schlant RC Dipyridamole in the treatment of angina pectoris. A double-blind evaluation. *JAMA* 1967;201:865-7 [[5340622](#)]

**Wirecki, 1967:**

Wirecki M Treatment of angina pectoris with dipyridamole: a long-term double blind study. *J Chronic Dis* 1967;20:139-45 [[5336520](#)]

**Becker, 1967:**

Becker MC. Angina pectoris: A double blind study with dipyridamole *Journal of the Newark Beth Israel Hospital* 1967;18:88-94

**EVOLVE, 2012:**

Meredith IT, Verheye S, Dubois CL, Dens J, Fajadet J, Carri D, Walsh S, Oldroyd KG, Varenne O, El-Jack S, Moreno R, Joshi AA, Allocco DJ, Dawkins KD Primary Endpoint Results of the EVOLVE Trial A Randomized Evaluation of a Novel Bioabsorbable Polymer-Coated, Everolimus-Eluting Coronary Stent. *J Am Coll Cardiol* 2012 Feb 3; [22341736] [10.1016/j.jacc.2011.12.016](https://doi.org/10.1016/j.jacc.2011.12.016)

**RITA 2, 1997:**

Coronary angioplasty versus medical therapy for angina: the second Randomised Intervention Treatment of Angina (RITA-2) trial. RITA-2 trial participants *Lancet* 1997;350:461-8 [9274581]

Henderson RA, Pocock SJ, Clayton TC, Knight R, Fox KA, Julian DG, Chamberlain DA Seven-year outcome in the RITA-2 trial: coronary angioplasty versus medical therapy *J Am Coll Cardiol* 2003;42:1161-70 [14522473]

**ACME, 1992:**

Parisi AF, Folland ED, Hartigan P A comparison of angioplasty with medical therapy in the treatment of single-vessel coronary artery disease. Veterans Affairs ACME Investigators *N Engl J Med* 1992;326:10-6 [1345754] [10.1056/NEJM199201023260102](https://doi.org/10.1056/NEJM199201023260102)

Hartigan PM, Giacomini JC, Folland ED, Parisi AF Two- to three-year follow-up of patients with single-vessel coronary artery disease randomized to PTCA or medical therapy (results of a VA cooperative study). Veterans Affairs Cooperative Studies Program ACME Investigators. Angioplasty Compared to Medicine *Am J Cardiol* 1998;82:1445-50 [9874045]

**ACME 2 (Folland), 1997:**

Folland ED, Hartigan PM, Parisi AF Percutaneous transluminal coronary angioplasty versus medical therapy for stable angina pectoris: outcomes for patients with double-vessel versus single-vessel coronary artery disease in a Veterans Affairs Cooperative randomized trial. Veterans Affairs ACME InvestigatorS *J Am Coll Cardiol* 1997;29:1505-11 [9180111]

Henderson RA, Pocock SJ, Clayton TC, Knight R, Fox KA, Julian DG, Chamberlain DA Seven-year outcome in the RITA-2 trial: coronary angioplasty versus medical therapy *J Am Coll Cardiol* 2003;42:1161-70 [14522473]

**ACIP, 1997:**

Davies RF, Goldberg AD, Forman S, Pepine CJ, Knatterud GL, Geller N, Sopko G, Pratt C, Deanfield J, Conti CR Asymptomatic Cardiac Ischemia Pilot (ACIP) study two-year follow-up: outcomes of patients randomized to initial strategies of medical therapy versus revascularization. *Circulation* 1997;95:2037-43 [9133513]

**INSPIRE, 2006:**

Mahmariyan JJ, Dakik HA, Filipchuk NG, Shaw LJ, Iskander SS, Ruddy TD, Keng F, Henzlova MJ, Allam A, Moy LA, Pratt CM An initial strategy of intensive medical therapy is comparable to that of coronary revascularization for suppression of scintigraphic ischemia in high-risk but stable survivors of acute myocardial infarction. *J Am Coll Cardiol* 2006;48:2458-67 [17174182]

**SWISSI II, 2007:**

Erne P, Schoenenberger AW, Burckhardt D, Zuber M, Kiowski W, Buser PT, Dubach P, Resink TJ, Pfisterer M Effects of percutaneous coronary interventions in silent ischemia after myocardial infarction: the SWISSI II randomized controlled trial. *JAMA* 2007;297:1985-91 [17488963]

**MASS, 1995:**

Hueb WA, Bellotti G, de Oliveira SA, Arie S, de Albuquerque CP, Jatene AD, Pileggi F The Medicine, Angioplasty or Surgery Study (MASS): a prospective, randomized trial of medical therapy, balloon angioplasty or bypass surgery for single proximal left anterior descending artery stenoses *J Am Coll Cardiol* 1995;26:1600-5 [7594092] [10.1016/0735-1097\(95\)00384-3](https://doi.org/10.1016/0735-1097(95)00384-3)

**Sievers, 1993:**

Sievers N, Hamm CW, Herzner A, Kuck KH Medical therapy versus PTCA: a prospective, randomized trial in patients with asymptomatic coronary single-vessel disease. Abstract. *Circulation*. 1993;88(suppl I):I-297 [0]

**de Jongste , 1994:**

de Jongste MJ, Hautvast RW, Hillege HL, Lie KI Efficacy of spinal cord stimulation as adjuvant therapy for intractable angina pectoris: a prospective, randomized clinical study. Working Group on Neurocardiology. *J Am Coll Cardiol* 1994;23:1592-7 [8195519]

Jessurun GA, DeJongste MJ, Hautvast RW, Tio RA, Brouwer J, van Lelieveld S, Crijns HJ Clinical follow-up after cessation of chronic electrical neuromodulation in patients with severe coronary artery disease: a prospective randomized controlled study on putative involvement of sympathetic activity. *Pacing Clin Electrophysiol* 1999;22:1432-9 [10588144]

**Lanza, 2005:**

Lanza GA, Sestito A, Sgueglia GA, Infusino F, Papacci F, Visocchi M, Ierardi C, Meglio M, Bellocchi F, Crea F Effect of spinal cord stimulation on spontaneous and stress-induced angina and 'ischemia-like' ST-segment depression in patients with cardiac syndrome X. *Eur Heart J* 2005;26:983-9 [[15642701](#)]

**SAPAT, 1992:**

Juul-Miller S, Edvardsson N, Jahnmatz B, Rosn A, Srensen S, Omblus R Double-blind trial of aspirin in primary prevention of myocardial infarction in patients with stable chronic angina pectoris. The Swedish Angina Pectoris Aspirin Trial (SAPAT) Group. *Lancet* 1992;340:1421-5 [[1360557](#)]

**Gupta et al, 1997:**

Gupta S, Leatham EW, Carrington D, Mendall MA, Kaski JC, Camm AJ Elevated Chlamydia pneumoniae antibodies, cardiovascular events, and azithromycin in male survivors of myocardial infarction. *Circulation* 1997 Jul 15;96:404-7 [[9244203](#)]

**ACADEMIC, 1999:**

Muhlestein JB, Anderson JL, Carlquist JF, Salunkhe K, Horne BD, Pearson RR, Bunch TJ, Allen A, Trehan S, Nielson C Randomized secondary prevention trial of azithromycin in patients with coronary artery disease: primary clinical results of the ACADEMIC study. *Circulation* 2000 Oct 10;102:1755-60 [[11023928](#)]

**STAMINA (Azithromycin), 2002:**

Stone AF, Mendall MA, Kaski JC, Edger TM, Risley P, Poloniecki J, Camm AJ, Northfield TC Effect of treatment for Chlamydia pneumoniae and Helicobacter pylori on markers of inflammation and cardiac events in patients with acute coronary syndromes: South Thames Trial of Antibiotics in Myocardial Infarction and Unstable Angina (STAMINA). *Circulation* 2002 Sep 3;106:1219-23 [[12208796](#)]

**AZACS, 2003:**

Cercek B, Shah PK, Noc M, Zahger D, Zeymer U, Matetzky S, Maurer G, Mahrer P Effect of short-term treatment with azithromycin on recurrent ischaemic events in patients with acute coronary syndrome in the Azithromycin in Acute Coronary Syndrome (AZACS) trial: a randomised controlled trial. *Lancet* 2003 Mar 8;361:809-13 [[12642046](#)]

**WIZARD, 2003:**

O'Connor CM, Dunne MW, Pfeffer MA, Muhlestein JB, Yao L, Gupta S, Benner RJ, Fisher MR, Cook TD Azithromycin for the secondary prevention of coronary heart disease events: the WIZARD study: a randomized controlled trial. *JAMA* 2003 Sep 17;290:1459-66 [[13129985](#)]

**ACES, 2005:**

Grayston JT, Kronmal RA, Jackson LA, Parisi AF, Muhlestein JB, Cohen JD, Rogers WJ, Crouse JR, Borrowdale SL, Schron E, Knirsch C Azithromycin for the secondary prevention of coronary events. *N Engl J Med* 2005 Apr 21;352:1637-45 [[15843666](#)]

**CLARIFY, 2001:**

Sinisalo J, Mattila K, Valtonen V, Anttonen O, Juvonen J, Melin J, Vuorinen-Markkola H, Nieminen MS Effect of 3 months of antimicrobial treatment with clarithromycin in acute non-q-wave coronary syndrome. *Circulation* 2002 Apr 2;105:1555-60 [[11927522](#)]

**CLARICOR, 2006:**

Jespersen CM, Als-Nielsen B, Damgaard M, Hansen JF, Hansen S, Hel OH, Hildebrandt P, Hilden J, Jensen GB, Kastrup J, Kolmos HJ, Kjeller E, Lind I, Nielsen H, Petersen L, Gluud C Randomised placebo controlled multicentre trial to assess short term clarithromycin for patients with stable coronary heart disease: CLARICOR trial. *BMJ* 2006 Jan 7;332:22-7 [[16339220](#)]

**Kinsella, 1962:**

KINSELLA D, TROUP W, MCGREGOR M Studies with a new coronary vasodilator drug: persantin. *Am Heart J* 1962;63:146-51 [[14456202](#)]

**Leiberman, 1964:**

LEIBERMAN A, GUGLIELMELLI S PERSANTIN- A DOUBLE BLIND STUDY. *Angiology* 1964;15:290-2 [[14170587](#)]

**Zion, 1961:**

ZION MM, BRADLOW BA A controlled clinical trial of 'persantin' (R A 8) in angina pectoris. *S Afr Med J* 1961;35:11-3 [[13788617](#)]

**Dewar, 1961:**

DEWAR HA, HORLER AR A clinical trial of Persantin and Crodimyl in the treatment of angina of effort. *Scott Med J* 1961;6:149-52 [[13722387](#)]

**Neumann, 1964:**

NEUMANN M, LUISADA AA EFFECT OF RAPID AND SLOW-ACTING "CORONARY" DRUGS ON PRECORDIAL PAIN OF THE AGED. *Am J Med Sci* 1964;247:156-63 [[14124704](#)]

**Foulds, 1960:**

FOULDS T, MACKINNON J Controlled double-blind trial of "persantin" in treatment of angina pectoris. *Br Med J* 1960;2:835 [[13824151](#)]

**Igloe, 1970:**

Igloe MC Treatment of angina pectoris with dipyridamole: a double-blind study. *J Am Geriatr Soc* 1970;18:233-41 [[4984849](#)]

**PROVE-IT, 2005:**

Cannon CP, Braunwald E, McCabe CH, Grayston JT, Muhlestein B, Giugliano RP, Cairns R, Skene AM Antibiotic treatment of Chlamydia pneumoniae after acute coronary syndrome. *N Engl J Med* 2005 Apr 21;352:1646-54 [[15843667](#)]

**Borer (CL2-009) 10mg, 2003:**

Borer JS, Fox K, Jaillon P, Lerebours G Antianginal and antiischemic effects of ivabradine, an I(f) inhibitor, in stable angina: a randomized, double-blind, multicentered, placebo-controlled trial. *Circulation* 2003 Feb 18;107:817-23 [[12591750](#)]

**BEAUTIFUL, 2008:**

Fox K, Ford I, Steg PG, Tendera M, Ferrari R Ivabradine for patients with stable coronary artery disease and left-ventricular systolic dysfunction (BEAUTIFUL): a randomised, double-blind, placebo-controlled trial. *Lancet* 2008 Sep 6;372:807-16 [[18757088](#)]

**SIGNIFY, 2014:**

Fox K, Ford I, Steg PG, Tardif JC, Tendera M, Ferrari R Ivabradine in Stable Coronary Artery Disease without Clinical Heart Failure. *N Engl J Med* 2014 Aug 31; [[25176136](#)] [10.1056/NEJMoa1406430](#)

**Borer (CL2-009) 20mg, 2003:****Borer (CL2-009) 5mg, 2003:**

Borer JS, Fox K, Jaillon P, Lerebours G *Circulation* 2003 Feb 18;107:817-23 [[12591750](#)]

**MARIZA, 2004:**

Chaitman BR, Skettino SL, Parker JO, Hanley P, Meluzin J, Kuch J, Pepine CJ, Wang W, Nelson JJ, Hebert DA, Wolff AA Anti-ischemic effects and long-term survival during ranolazine monotherapy in patients with chronic severe angina. *J Am Coll Cardiol* 2004;43:1375-82 [[15093870](#)]

**RAN080, 2005:**

Rousseau MF, Pouleur H, Cocco G, Wolff AA Comparative efficacy of ranolazine versus atenolol for chronic angina pectoris. *Am J Cardiol* 2005;95:311-6 [[15670536](#)]

**Murphy, 2003:**

Murphy J, Wright RS, Gussak I, Williams B, Daly RN, Cain VA, Pieniaszek HJ, Sy SK, Ebling W, Simonson K, Wilcox RA, Kopecky SL The use of roxifiban (DMP754), a novel oral platelet glycoprotein IIb/IIIa receptor inhibitor, in patients with stable coronary artery disease. *Am J Cardiovasc Drugs* 2003;3:101-12 [[14727937](#)]

**Eddicks, 2007:**

Eddicks S, Maier-Hauff K, Schenk M, Mller A, Baumann G, Theres H Thoracic spinal cord stimulation improves functional status and relieves symptoms in patients with refractory angina pectoris: the first placebo-controlled randomised study. *Heart* 2007;93:585-90 [[17237126](#)]

**BEAUTIFUL (angina subgroup), :**

Fox K, Ford I, Steg PG, Tendera M, Robertson M, Ferrari R Relationship between ivabradine treatment and cardiovascular outcomes in patients with stable coronary artery disease and left ventricular systolic dysfunction with limiting angina: a subgroup analysis of the randomized, controlled BEAUTIFUL trial. *Eur Heart J* 2009 Oct;30:2337-45 [[19720635](#)]

**CARISA 1000mg, 2004:**

Chaitman BR, Pepine CJ, Parker JO, Skopal J, Chumakova G, Kuch J, Wang W, Skettino SL, Wolff AA Effects of ranolazine with atenolol, amlodipine, or diltiazem on exercise tolerance and angina frequency in patients with severe chronic angina: a randomized controlled trial. *JAMA* 2004 Jan 21;291:309-16 [[14734593](#)]

**ERICA, 2006:**

Stone PH, Gratsiansky NA, Blokhin A, Huang IZ, Meng L Antianginal efficacy of ranolazine when added to treatment with amlodipine: the ERICA (Efficacy of Ranolazine in Chronic Angina) trial. *J Am Coll Cardiol* 2006 Aug 1;48:566-75 [[16875985](#)]

**CL3-018 10mg, 3000:**

unpublished

**CL3-018 15mg, 3000:**

unpublished

**ASSOCIATE (Tardif), 2009:**

Tardif JC, Ponikowski P, Kahan T Efficacy of the I(f) current inhibitor ivabradine in patients with chronic stable angina receiving beta-blocker therapy: a 4-month, randomized, placebo-controlled trial. *Eur Heart J* 2009 Mar;30:540-8 [[19136486](#)]

**Nordic Bifurcation Study, 0:**

ongoing trial NCT00376571

**FEMH-93005, 0:**

ongoing trial NCT00190099

**CL3-023 (15mg), 0:**

unpublished

**CL3-023 (20mg), 0:**

unpublished

**6 hypertension**

Trial	Treatments	Patients	Trials design and methods
<b>aliskiren vs amlodipine</b>			
<a href="#">ACCELERATE , 2011</a> [NCT00797862] n=NA follow-up:	-	essential hypertension, were aged 18 years or older, and had systolic blood pressure between 150 and 180 mmHg	
<b>ARBs vs control</b>			
<a href="#">Suzuki , 2008</a> n=183/183 follow-up:	ARBs (valsartan, candesartan, and losartan) versus no ARBs	patients with diabetes and chronic kidney disease on dialysis	Parallel groups open
<b>atenolol vs control</b>			
<a href="#">Coope , 1986</a> n=419/465 follow-up: 44y	atenolol and bendrofluazide , Atenolol versus Open control	patients aged 60 to 79 years	Parallel groups open
<a href="#">Coope (subgroup ) , 1986</a> n=3/4 follow-up: 38y	atenolol and bendrofluazide versus control	patients aged 60 to 79 years	double-blind
<b>candesartan vs control</b>			
<a href="#">Takahashi , 2006</a> n=43/37 follow-up: 19.4 months	candesartan versus control	patients on chronic haemodialysis in stable condition and with no clinical evidence of cardiac disorders	Parallel groups open
<b>captopril or atenolol vs control</b>			

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>UKPDS 38 , 1998</b> n=758/390 follow-up: 8.4y (median)	tight control of blood pressure aiming at a BP <150/85 (with the use of captopril or atenolol as main treatment, other treatment were added if the control criteria were not met) versus less tight control aiming at a blood pressure of <180/105 (avoiding treatment with ACE inhibitors or beta-blockers)	hypertensive patients with type 2 diabetes	Parallel groups open UK
<b>thiazide diuretics vs control</b>			
<b>Carter , 1970</b> n=50/49 follow-up: 3.6 y	thiazide versus ?	-	NA Open
<b>Oslo (Hegeland) , 1980</b> n=406/379 follow-up: 5.5 y	step 1: hydrochlorothiazide 50mg/d, step 2: alpha methyl dopa 250-500mg x2/d or propranolol 40-160mg x2/d, versus no treatment	men, aged 40 to 49 years, without target organ damage, with systolic blood pressures between 150 and 179 mm Hg and diastolic blood pressure below 110 mm Hg	parallel group Open Oslo
<b>ANBPS (Australian) , 1980</b> n=1721/1706 follow-up: 4 y	step 1: chlorothiazide 500 mg/d, step 2: chlorothiazide 500mg x2/d or methyl dopa, propranolol, pindolol added, step 3: hydralazine or clonidine added versus placebo (without adjustment according to the BP!)	-	parallel group Double blind Australia
<b>candesartan vs conventional treatment</b>			
<b>E-COST , 2005</b> n=1053/995 follow-up:	candesartan, 2 to 12 mg daily versus conventional antihypertensive drugs other than angiotensin converting enzyme inhibitors or ARBs	Japanese essential hypertensive subjects (sitting blood pressure 140-180/90-110 mmHg) aged 35-79 years	Parallel groups single-blind Japan
<b>E-COST-R , 2005</b> n=69/72 follow-up:	candesartan versus conventional treatment	hypertensive subjects 60 to 75 years old with non-diabetic chronic renal insufficiency	Parallel groups open
<b>HIJ-CREATE , 2009</b> n=1024/1025 follow-up: 4.2 y (median)	angiotensin II receptor blocker-based therapy versus non-angiotensin II receptor blocker-based therapy	patients with angiographically documented coronary artery disease and hypertension	Parallel groups open Japan
<b>angioplasty vs medical therapy</b>			

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>EMMA , 1998</b> n=23/26 follow-up: 6 months	angioplasty versus antihypertensive drug treatment	hypertensive patients with atherosclerotic renal artery stenosis.	Parallel groups open France
<b>SNRASCg , 1998</b> n=25/30 follow-up: 12 months	percutaneous transluminal angioplasty versus medical therapy	hypertensive patients with unilateral or bilateral disease	Parallel groups United Kingdom
<b>DRASTIC , 2000</b> n=56/50 follow-up: 12 months	percutaneous transluminal renal angioplasty versus drug therapy	patients with hypertension who had atherosclerotic renal-artery stenosis (defined as a decrease in luminal diameter of 50 percent or more) and a serum creatinine concentration of 2.3 mg per deciliter (200 micromol per liter) or less	Parallel groups open Netherlands
<b>ASTRAL , 2009</b> n=403/403 follow-up: 33.6 months	revascularization in addition to medical therapy versus medical therapy alone	patients with atherosclerotic renovascular disease	Parallel groups open United Kingdom, Australia, New Zealand
<b>STAR , 2009</b> n=64/76 follow-up: 24 months	stent placement and medical treatment versus medical treatment alone (antihypertensive treatment, statin, aspirin)	patients with atherosclerotic renal artery stenosis and impaired renal function	Parallel groups open Netherlands, France
<b>NITER , 2009</b> <i>unpublished</i> n=28/24 follow-up: 43 months	-	-	Italy
<b>ACE inhibitors vs placebo</b>			
<b>HOPE (diabetic subgroup) , 2000</b> n=1808/1759 follow-up: 4.5 years	ramipril 10 mg once per day orally versus placebo	patients with diabetes (sub group), aged 55 years or older, who had a previous cardiovascular event or at least one other cardiovascular risk factor, no clinical proteinuria, heart failure, or low ejection fraction	Factorial plan double-blind North, South america, Europe
<b>aliskiren vs placebo</b>			
<b>AVOID , 2008</b> [NCT00097955] n=301/298 follow-up: 6 months	aliskiren (150 mg daily for 3 months, followed by an increase in dosage to 300 mg daily for another 3 months) versus placebo	patients with hypertension and type 2 diabetes with nephropathy	Parallel groups double blind 15 countries
<b>amlodipine vs placebo</b>			
<b>IDNT (amlodipine vs pbo) , 2001</b> n=567/569 follow-up: 26	Amlodipine 10mg/d versus placebo	hypertensive patients with nephropathy due to type 2 diabetes	Parallel groups Double blind

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>IDNT (amlodipine vs PBO) , 2001</b> n=567/569 follow-up: 2.6 years	Amlodipine 10 mg daily versus placebo	hypertensive patients with nephropathy due to type 2 diabetes	Parallel groups double-blind Worldwide
<b>Tepel et al , 2008</b> [NCT00124969] n=123/128 follow-up: 19 montsh median (8-30)	Amlodipine 10 mg/day versus matched placebo	hypertensive haemodialysis patients	double blind
<b>aspirin vs placebo</b>			
<b>HOT , 1998</b> n=9399/9391 follow-up: mean 3.8 y (range 3.3-4.9y)	aspirin 75 mg daily versus placebo	patients aged 50-80 with hypertension and diastolic blood pressure between 100 mmHG and 115 mmHG	Factorial plan Double blind Europe, North and South America, and Asia
<b>atenolol vs placebo</b>			
<b>MRC I (vs placebo) , 1985</b> n=4403/8654 follow-up: 5.5y	Propranolol versus Placebo	men and women aged 35-64 yearswith mild hypertension (diastolic pressure 90-109 mm Hg	Parallel groups double blind
<b>MRC old (vs placebo) , 1992</b> n=1102/2213 follow-up: 5.8y	Atenolol versus Placebo	patients aged 65-74	double blind UK
<b>Dutch TIA , 1993</b> n=732/741 follow-up: 26y	Atenolol 50mg/d versus Placebo	aspirin-treated patients with transient ischemic attack or nondisabling ischemic stroke	double blind
<b>TEST , 1995</b> n=372/348 follow-up: 26y	Atenolol versus Placebo	post stroke	
<b>atorvastatin vs placebo</b>			
<b>ASCOT , 2003</b> n=5168/5137 follow-up: 3.3 years	atorvastatin 10mg/d versus placebo	hypertensive patients aged 40-79 years with at least three other cardiovascular risk factors	Parallel groups double blind UK et Scandinavie
<b>beta-blockers + diuretics vs placebo</b>			
<b>CASTEL (subgroup ) , 1994</b> n=47/50 follow-up: 68y	active antihypertensive therapy (thiazide or beta-blockers) versus control	-	open
<b>beta-blockers or diuretics vs placebo</b>			

continued...



<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>STOP (subgroup) , 1991</b> n=122/113 follow-up: 21 y	active antihypertensive therapy (three beta-blockers and one diuretic) versus placebo	hypertensive Swedish men and women aged 70-84 years	double-blind Sweden
<b>candesartan vs placebo</b>			
<b>TROPHY , 2006</b> [NCT00227318] n=409/400 follow-up: 4y	candesartan during 2y followed by 2y of placebo versus placebo	subjects with repeated measurements of systolic pressure of 130 to 139 mm Hg and diastolic pressure of 89 mm Hg or lower, or systolic pressure of 139 mm Hg or lower and diastolic pressure of 85 to 89 mm Hg	Parallel groups double-blind USA
<b>SCOPE , 2003</b> n=2477/2460 follow-up: 3.7 y (mean)	candesartan, 816 mg once daily (target 160/90) versus placebo	patients aged 70-89 years, with systolic blood pressure 160-179 mmHg, and/or diastolic blood pressure 90-99 mmHg, and a Mini Mental State Examination (MMSE) test score >24	Parallel groups double-blind 15 countries
<b>carvedilol vs placebo</b>			
<b>Cice et al , 2003</b> n=58/56 follow-up: 12 months	65279;Carvedilol 50 mg/day versus matched placebo	dialysis patients with dilated cardiomyopathy	
<b>Nakao et al , 2007</b> n=57/51	Carvedilol 20 mg/day versus matched placebo	-	
<b>chlorthalidone vs placebo</b>			
<b>SHEP-pilot , 1989</b> n=443/108 follow-up: 2.8y	chlorthalidone versus placebo	elderly participants with untreated blood pressures of greater than 160/less than 90 mm Hg	double blind
<b>VA-NHLBI , 1977</b> n=508/504 follow-up: 1.4 y	chlorthalidone 50mg/d versus placebo	patients aged 21 to 50 years with diastolic BP between 85 to 105 mm Hg	Double aveugle USA
<b>SHEP , 1991</b> [NCT00000514] n=2365/2371 follow-up: 4.4 y	chlorthalidone, 12.5 mg/d , chlorthalidone, 12.5 mg/d , chlorthalidone, 12.5 mg/d versus placebo	patients aged 60 years and above with Systolic BP between 160 and 219 mm Hg and diastolic BP less than 90 mm Hg	Double blind
<b>SHEP (diabetic subgroup) , 1996</b> n=283/300 follow-up: 5 year	low dose of chlorthalidone (12.5-25.0 mg/d) with a step-up to atenolol (25.0-50.0 mg/d) or reserpine (0.05-0.10 mg/d) if needed versus placebo	men and women aged 60 years and older , non-insulin-treated diabetic (sub group) patients with isolated systolic hypertension (systolic BP $\geq$ 160 mm Hg; diastolic BP, <90 mm Hg)	Parallel groups double-blind
<b>SHEP-P (subgroup) , 1989</b> n=70/15 follow-up: 28y	chlorthalidone versus placebo	elderly participants with untreated blood pressures of greater than 160/less than 90 mm Hg	double-blind

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>SHEP (subgroup) , 1991</b> n=331/319 follow-up: 42y	chlorthalidone, 12.5 mg/d for step 1 versus placebo	patients aged 60 years and above	double blind
<b>darusentan vs placebo</b>			
<b>DORADO-AC</b> n=NA follow-up:	-	-	
<b>DORADO , 2009</b> [NCT00330369] n=247/132 follow-up: 14 weeks	darusentan 50 mg, 100 mg or 300 mg versus placebo	patients with treatment-resistant hypertension	Parallel groups double blind North and South America, Europe, New Zealand, Australia
<b>deserpidine +methylclothiazide vs placebo</b>			
<b>HSCS , 1974</b> n=233/219 follow-up: 2.3y	deserpidine 1mg/d + methylclothiazide 10mg/d versus placebo	stroke	Parallel groups Double blind USA
<b>diuretic and rauwolfia serpentina vs placebo</b>			
<b>USPHS , 1977</b> n=193/196 follow-up: 7.0 y	diuretic and rauwolfia serpentina versus placebo	subjects, ages 21-55, with diastolic blood pressures between 90 and 115 mm Hg	double blind
<b>fluvastatin vs placebo</b>			
<b>HYRIM , 2005</b> n=283/285 follow-up: 4 year	fluvastatin 40 mg daily versus placebo	drug-treated hypertensive men aged 40-74 years with total cholesterol 4.5-8.0 mmol/L, triglycerides <4.5 mmol/L, body mass index 25-35 kg/m <sup>2</sup> , and a sedentary lifestyle	Factorial plan double blind Norway
<b>hydrochlorothiazide vs placebo</b>			
<b>EWPHE (subgroup) , 1985</b> n=70/85 follow-up: 31y	hydrochlorothiazide + triamterene versus placebo	patients over the age of 60	double-blind
<b>hydrochlorothiazide + amiloride vs placebo</b>			
<b>MRC old , 1992</b> n=1081/2213 follow-up:	-	hypertensive patients aged 64-75	
<b>hydrochlorothiazide + triamterene vs placebo</b>			
<b>Kuramoto , 1981</b> n=44/47 follow-up: 4.0y	hydrochlorothiazide + triamterene versus placebo	patients over the age of 60 with sitting diastolic blood pressure on placebo treatment in the range 90-119 mm Hg and a systolic pressure in the range 160-239 mm Hg	double blind

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>EWPHE , 1985</b> n=416/424 follow-up: 4.3 y	hydrochlorothiazide + triamterene , hydrochlorothiazide + triamterene versus placebo	patients over the age of 60 with sitting diastolic blood pressure on placebo treatment in the range 90-119 mm Hg and a systolic pressure in the range 160-239 mm Hg	Double blind
<b>indapamide vs placebo</b>			
<b>HYVET , 2008</b> [NCT00122811] n=1933/1912 follow-up: 1.8y (median)	indapamide sustained release 1.5 mg/d + perindopril 2-4mg/d to obtain SBP<150 and DBP<80 versus placebo	patients 80 years or older with persistent hypertension defined as a sustained systolic BP of 160 mm Hg or higher	Parallel groups Double blind Western and Eastern Europe, China, Australasia, and North Africa
<b>PATS , 1995</b> n=2841/2841 follow-up: 2y	indapamide 2.5 mg/d versus placebo	-	Parallel groups Double blind China
<b>irbesartan vs placebo</b>			
<b>IDNT (irbesartan vs pbo) , 2001</b> n=579/569 follow-up: 2.6 y	Irbesartan 300mg/d (target 135/85) versus placebo	hypertensive patients with nephropathy due to type 2 diabetes	Parallel groups double-blind worldwide
<b>IRMA 2 , 2001</b> n=404/207 follow-up: 2 years	irbesartan 150 mg daily or 300 mg daily versus placebo	hypertensive patients with type 2 diabetes and microalbuminuria	Parallel groups double-blind multinational
<b>IDNT (irbesartan vs pbo) , 2001</b> n=579/569 follow-up: 2.6 years	Irbesartan 300 mg daily versus placebo	hypertensive patients with nephropathy due to type 2 diabetes	Parallel groups double blind Worldwide
<b>IPDM (150mg) , 2001</b> n=195/201 follow-up: 2 years	irbesartan 150 mg daily versus placebo	hypertensive patients with type 2 diabetes and microalbuminuria	Parallel groups double-blind Worldwide
<b>losartan vs placebo</b>			
<b>RENAAL , 2001</b> n=751/762 follow-up: 3.4 years	Losartan 50 to 100 mg once daily versus placebo	patients with type 2 diabetes and nephropathy	Parallel groups double-blind
<b>RENAAL , 2001</b> n=751/762 follow-up: 3.4 y	losartan 50 to 100 mg once daily versus placebo	patients with type 2 diabetes and nephropathy	Parallel groups double-blind America, Europe, Asia
<b>telmisartan vs placebo</b>			

continued...

Trial	Treatments	Patients	Trials design and methods
PROPHESSE , 2008 [NCT00153062] n=10146/10186 follow-up: 2.5 y	telmisartan 80 mg daily versus placebo	patients who recently had an ischemic stroke	Factorial plan double blind 35 countries
Cice et al , 2006 n=151/152	Telmisartan 80 mg/day versus matched placebo	-	

More details and results :

- anti hypertensive agents for hypertension in elderly (60 years and more) at <http://www.trialresultscenter.org/go-Q9>
- anti hypertensive agents for hypertension in diabetic patients at <http://www.trialresultscenter.org/go-Q10>
- anti hypertensive agents for hypertension in all type of patient at <http://www.trialresultscenter.org/go-Q13>
- anti hypertensive agents for hypertension in very ederly (80 and more) at <http://www.trialresultscenter.org/go-Q14>
- anti hypertensive agents for hypertension in nephropathy at <http://www.trialresultscenter.org/go-Q19>
- anti hypertensive agents for hypertension in post stroke at <http://www.trialresultscenter.org/go-Q20>
- angiotensin-receptor blockers for hypertension in all diseases requiring ACEi (HF, CHD, HT,...) at <http://www.trialresultscenter.org/go-Q125>
- anti hypertensive agents for hypertension in patients undergoing dialysis at <http://www.trialresultscenter.org/go-Q281>
- renin inhibitor for hypertension in all type of patients at <http://www.trialresultscenter.org/go-Q309>
- renin inhibitor for hypertension in diabetic patients at <http://www.trialresultscenter.org/go-Q310>
- intensive blood pressure control for hypertension in all type of patients at <http://www.trialresultscenter.org/go-Q336>
- intensive blood pressure control for hypertension in diabetic patients at <http://www.trialresultscenter.org/go-Q343>
- intensive blood pressure control for hypertension in non diabetic patients at <http://www.trialresultscenter.org/go-Q344>
- anti hypertensive agents for hypertension in patients with treatment-resistant hypertension at <http://www.trialresultscenter.org/go-Q374>
- anti hypertensive agents for hypertension in subjects with pre-hypertension at <http://www.trialresultscenter.org/go-Q404>
- antiplatelets drug for hypertension in all type of patients at <http://www.trialresultscenter.org/go-Q407>
- cholesterol lowering intervention for hypertension in all type of patients at <http://www.trialresultscenter.org/go-Q458>
- intensive blood pressure control for hypertension in patients with chronic kidney disease at <http://www.trialresultscenter.org/go-Q495>
- angioplasty for hypertension in all type of patients at <http://www.trialresultscenter.org/go-Q496>
- anti hypertensive agents for hypertension in uncomplicated hypertension at <http://www.trialresultscenter.org/go-Q685>

## References

### ACCELERATE, 2011:

Brown MJ, McInnes GT, Papst CC, Zhang J, Macdonald TM Aliskiren and the calcium channel blocker amlodipine combination as an initial treatment strategy for hypertension control (ACCELERATE): a randomised, parallel-group trial. Lancet 2011 Jan 12;; [21236483] 10.1016/S0140-6736(10)62003-X

### Suzuki, 2008:

Suzuki H, Kanno Y, Sugahara S, Ikeda N, Shoda J, Takenaka T, Inoue T, Araki R Effect of angiotensin receptor blockers on cardiovascular events in patients undergoing hemodialysis: an open-label randomized controlled trial. Am J Kidney Dis 2008;52:501-6 [18653268] 10.1053/j.ajkd.2008.04.031

**Coope, 1986:**

Coope J, Warrender TS Randomised trial of treatment of hypertension in elderly patients in primary care. *Br Med J (Clin Res Ed)* 1986 Nov 1;293:1145-51 [[3094811](#)]

**Coope (subgroup ), 1986:**

Coope J, Warrender TS Randomised trial of treatment of hypertension in elderly patients in primary care. *Br Med J (Clin Res Ed)* 1986;293:1145-51 [[3094811](#)]

**Takahashi, 2006:**

Takahashi A, Takase H, Toriyama T, Sugiura T, Kurita Y, Ueda R, Dohi Y Candesartan, an angiotensin II type-1 receptor blocker, reduces cardiovascular events in patients on chronic haemodialysis—a randomized study. *Nephrol Dial Transplant* 2006;21:2507-12 [[16766543](#)] [10.1093/ndt/gfl293](#)

**UKPDS 38, 1998:**

Efficacy of atenolol and captopril in reducing risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 39. UK Prospective Diabetes Study Group. *BMJ* 1998;317:713-20 [[9732338](#)]

Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38. UK Prospective Diabetes Study Group. *BMJ* 1998;317:703-13 [[9732337](#)]

**Carter, 1970:**

Carter AB Hypotensive therapy in stroke survivors. *Lancet* 1970;1:485-9 [[4190177](#)]

**Oslo (Hegeland), 1980:**

Helgeland A Treatment of mild hypertension: a five year controlled drug trial. The Oslo study. *Am J Med* 1980;69:725-32 [[7001898](#)]

**ANBPS (Australian ), 1980:**

The Australian therapeutic trial in mild hypertension. Report by the Management Committee. *Lancet* 1980;1:1261-7 [[6104081](#)]

**E-COST, 2005:**

Suzuki H, Kanno Y Effects of candesartan on cardiovascular outcomes in Japanese hypertensive patients. *Hypertens Res* 2005;28:307-14 [[16138560](#)] [10.1291/hyPRES.28.307](#)

**E-COST-R, 2005:**

Nakamura T, Kanno Y, Takenaka T, Suzuki H An angiotensin receptor blocker reduces the risk of congestive heart failure in elderly hypertensive patients with renal insufficiency. *Hypertens Res* 2005;28:415-23 [[16156505](#)] [10.1291/hyPRES.28.415](#)

**HIJ-CREATE, 2009:**

Kasanuki H, Hagiwara N, Hosoda S, Sumiyoshi T, Honda T, Haze K, Nagashima M, Yamaguchi J, Origasa H, Urashima M, Ogawa H Angiotensin II receptor blocker-based vs. non-angiotensin II receptor blocker-based therapy in patients with angiographically documented coronary artery disease and hypertension: the Heart Institute of Japan Candesartan Randomized Trial for Evaluation in Coronary Artery Disease (HIJ-CREATE). *Eur Heart J* 2009;30:1203-12 [[19346521](#)] [10.1093/eurheartj/ehp101](#)

**EMMA, 1998:**

Plouin PF, Chatellier G, Darn B, Raynaud A Blood pressure outcome of angioplasty in atherosclerotic renal artery stenosis: a randomized trial. Essai Multicentrique Medicaments vs Angioplastie (EMMA) Study Group. *Hypertension* 1998;31:823-9 [[9495267](#)]

**SNRASC, 1998:**

Webster J, Marshall F, Abdalla M, Dominiczak A, Edwards R, Isles CG, Loose H, Main J, Padfield P, Russell IT, Walker B, Watson M, Wilkinson R Randomised comparison of percutaneous angioplasty vs continued medical therapy for hypertensive patients with atheromatous renal artery stenosis. Scottish and Newcastle Renal Artery Stenosis Collaborative Group. *J Hum Hypertens* 1998;12:329-35 [[9655655](#)]

**DRASTIC, 2000:**

van Jaarsveld BC, Krijnen P, Pieterman H, Derckx FH, Deinum J, Postma CT, Dees A, Woittiez AJ, Bartelink AK, Man in 't Veld AJ, Schalekamp MA The effect of balloon angioplasty on hypertension in atherosclerotic renal-artery stenosis. Dutch Renal Artery Stenosis Intervention Cooperative Study Group. *N Engl J Med* 2000;342:1007-14 [[10749962](#)] [10.1056/NEJM200004063421403](#)

**ASTRAL, 2009:**

Wheatley K, Ives N, Gray R, Kalra PA, Moss JG, Baigent C, Carr S, Chalmers N, Eadington D, Hamilton G, Lipkin G, Nicholson A, Scoble J Revascularization versus medical therapy for renal-artery stenosis. *N Engl J Med* 2009;361:1953-62 [[19907042](#)] [10.1056/NEJMoa0905368](#)

**STAR, 2009:**

Bax L, Woittiez AJ, Kouwenberg HJ, Mali WP, Buskens E, Beek FJ, Braam B, Huysmans FT, Schultze Kool LJ, Rutten MJ, Doorenbos CJ, Aarts JC, Rabelink TJ, Plouin PF, Raynaud A, van Montfrans GA, Reekers JA, van den Meiracker AH, Pattynama PM, van de Ven PJ, Stent placement in patients with atherosclerotic renal artery stenosis and impaired renal function: a randomized trial. *Ann Intern Med* 2009;150:840-8, W150-1 [[19414832](#)]

**NITER, 2009:**

unpublished

Scarpioni R, Michieletti E, Pavone L, et al. Atherosclerotic renovascular disease (ARVD): medical therapy plus renal artery stenting (PRTS), compared with medical therapy alone, do not offer more chances in preventing C-V events or the progression of renal failure. Preliminary results of a prospective, multicenter and randomized trial Abstract World Congress of Nephrology; May 22, 2009; Milan, Italy; 2009.

**HOPE (diabetic subgroup), 2000:**

Effects of ramipril on cardiovascular and microvascular outcomes in people with diabetes mellitus: results of the HOPE study and MICRO-HOPE substudy. Heart Outcomes Prevention Evaluation Study Investigators. Lancet 2000;355:253-9 [10675071]

Yusuf S, Sleight P, Pogue J, Bosch J, Davies R, Dagenais G Effects of an angiotensin-converting-enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients. The Heart Outcomes Prevention Evaluation Study Investigators. N Engl J Med 2000;342:145-53 [10639539]

**AVOID, 2008:**

Parving HH, Persson F, Lewis JB, Lewis EJ, Hollenberg NK Aliskiren combined with losartan in type 2 diabetes and nephropathy. N Engl J Med 2008;358:2433-46 [18525041]

**IDNT (amlodipine vs pbo), 2001:**

Lewis EJ, Hunsicker LG, Clarke WR, Berl T, Pohl MA, Lewis JB, Ritz E, Atkins RC, Rohde R, Raz I Renoprotective effect of the angiotensin-receptor antagonist irbesartan in patients with nephropathy due to type 2 diabetes. N Engl J Med 2001;345:851-60 [11565517]

**IDNT (amlodipine vs PBO), 2001:**

Lewis EJ, Hunsicker LG, Clarke WR, Berl T, Pohl MA, Lewis JB, Ritz E, Atkins RC, Rohde R, Raz I Renoprotective effect of the angiotensin-receptor antagonist irbesartan in patients with nephropathy due to type 2 diabetes. N Engl J Med 2001;345:851-60 [11565517]

Hunsicker LG, Atkins RC, Lewis JB, Braden G, de Crespigny PJ, DeFerrari G, Drury P, Locatelli F, Wiegmann TB, Lewis EJ Impact of irbesartan, blood pressure control, and proteinuria on renal outcomes in the Irbesartan Diabetic Nephropathy Trial. Kidney Int Suppl 2004;:S99-101 [15485429] 10.1111/j.1523-1755.2004.09223.x

POHL, MA, CORDONNIER, DJ, SPITALOWITZ, S, et al, FOR THE COLLABORATIVE STUDY GROUP Impact of angiotensin receptor blockade with irbesartan on renal function at different systolic blood pressure (SBP) levels in type 2 diabetic nephropathy. J Am Soc Nephrol 2002 13: 650A,

Pohl MA, Blumenthal S, Cordonnier DJ, De Alvaro F, Deferrari G, Eisner G, Esmatjes E, Gilbert RE, Hunsicker LG, de Faria JB, Mangili R, Moore J Jr, Reisin E, Ritz E, Scherthaner G, Spitalowitz S, Tindall H, Rodby RA, Lewis EJ Independent and additive impact of blood pressure control and angiotensin II receptor blockade on renal outcomes in the irbesartan diabetic nephropathy trial: clinical implications and limitations. J Am Soc Nephrol 2005;16:3027-37 [16120823] 10.1681/ASN.2004110919

**Tepel et al, 2008:**

Tepel M, Hopfenmueller W, Scholze A, Maier A, Zidek W Nephrol Dial Transplant 2008;23:3605-12 [18511605] 10.1093/ndt/gfn304

**HOT, 1998:**

Hansson L, Zanchetti A, Carruthers SG, Dahlof B, Elmfeldt D, Julius S, Menard J, Rahn KH, Wedel H, Westerling S Effects of intensive blood-pressure lowering and low-dose aspirin in patients with hypertension: principal results of the Hypertension Optimal Treatment (HOT) randomised trial. HOT Study Group. Lancet 1998 Jun 13;351:1755-62 [9635947]

Hansson L, Zanchetti A The Hypertension Optimal Treatment (HOT) Study-patient characteristics: randomization, risk profiles, and early blood pressure results. Blood Press 1994;3:322-7 [7866597]

**MRC I (vs placebo), 1985:**

MRC trial of treatment of mild hypertension: principal results. Medical Research Council Working Party. Br Med J (Clin Res Ed) 1985 Jul 13;291:97-104 [2861880]

**MRC old (vs placebo), 1992:**

Medical Research Council trial of treatment of hypertension in older adults: principal results. MRC Working Party. BMJ 1992 Feb 15;304:405-12 [1445513]

**Dutch TIA, 1993:**

Trial of secondary prevention with atenolol after transient ischemic attack or nondisabling ischemic stroke. The Dutch TIA Trial Study Group. Stroke 1993 Apr;24:543-8 [8465360]

**TEST, 1995:**

Eriksson S, Olofsson BO, Wester PO. imag Atenolol in the secondary prevention after stroke Cerebrovasc Dis 1995; 5: 2125

**ASCOT, 2003:**

Sever PS, Dahlof B, Poulter NR, Wedel H, Beevers G, Caulfield M, Collins R, Kjeldsen SE, Kristinsson A, McInnes GT, Mehlsen J, Nieminen M, O'Brien E, Ostergren J, Prevention of coronary and stroke events with atorvastatin in hypertensive patients who have average or lower-than-average cholesterol concentrations, in the Anglo-Scandinavian Cardiac Outcomes Trial-Lipid Lowering Arm (ASCOT-LLA): a multicentre randomised controlled trial. *Lancet* 2003; 361:1149-58 [[12686036](#)]

**CASTEL (subgroup), 1994:**

Casiglia E, Spolaore P, Mazza A, Ginocchio G, Colangeli G, Onesto C, Di Menza G, Pegoraro L, Ambrosio GB Effect of two different therapeutic approaches on total and cardiovascular mortality in a Cardiovascular Study in the Elderly (CASTEL). *Jpn Heart J* 1994;35:589-600 [[7830324](#)]

**STOP (subgroup), 1991:**

Dahlf B, Lindholm LH, Hansson L, Scherstn B, Ekblom T, Wester PO Morbidity and mortality in the Swedish Trial in Old Patients with Hypertension (STOP-Hypertension) *Lancet* 1991;338:1281-5 [[1682683](#)]

**TROPHY, 2006:**

Julius S, Nesbitt SD, Egan BM, Weber MA, Michelson EL, Kaciroti N, Black HR, Grimm RH Jr, Messerli FH, Oparil S, Schork MA Feasibility of treating prehypertension with an angiotensin-receptor blocker. *N Engl J Med* 2006;354:1685-97 [[16537662](#)] [10.1056/NEJMoa060838](#)

**SCOPE, 2003:**

Saxby BK, Harrington F, Wesnes KA, McKeith IG, Ford GA Candesartan and cognitive decline in older patients with hypertension: a substudy of the SCOPE trial. *Neurology* 2008;70:1858-66 [[18458219](#)] [10.1212/01.wnl.0000311447.85948.78](#)

Lithell H, Hansson L, Skoog I, Elmfeldt D, Hofman A, Olofsson B, Trenkwalder P, Zanchetti A The Study on Cognition and Prognosis in the Elderly (SCOPE): principal results of a randomized double-blind intervention trial. *J Hypertens* 2003;21:875-86 [[12714861](#)] [10.1097/01.hjh.0000059028.82022.89](#)

**Cice et al, 2003:**

Cice G, Ferrara L, D'Andrea A, D'Isa S, Di Benedetto A, Cittadini A, Russo PE, Golino P, Calabr R *J Am Coll Cardiol* 2003;41:1438-44 [[12742278](#)]

**Nakao et al, 2007:**

Nakao N, Hasegawa H, Fujimori A, Seno H, Toriyama T, *J Am Soc Nephrol* 2007;18 (suppl): 709A [[0](#)]

**SHEP-pilot, 1989:**

Perry HM Jr, Smith WM, McDonald RH, Black D, Cutler JA, Furberg CD, Greenlick MR, Kuller LH, Schnaper HW, Schoenberger JA Morbidity and mortality in the Systolic Hypertension in the Elderly Program (SHEP) pilot study. *Stroke* 1989 Jan;20:4-13 [[2911834](#)]

**VA-NHLBI, 1977:**

Evaluation of drug treatment in mild hypertension: VA-NHLBI feasibility trial. Plan and preliminary results of a two-year feasibility trial for a multicenter intervention study to evaluate the benefits versus the disadvantages of treating mild hypertension. Prepared for the Veterans Administration-National Heart, Lung, and Blood Institute Study Group for Evaluating Treatment in Mild Hypertension. *Ann N Y Acad Sci* 1978;304:267-92 [[360921](#)]

**SHEP, 1991:**

Prevention of stroke by antihypertensive drug treatment in older persons with isolated systolic hypertension. Final results of the Systolic Hypertension in the Elderly Program (SHEP). SHEP Cooperative Research Group. *JAMA* 1991;265:3255-64 [[2046107](#)]

Kostis JB, Davis BR, Cutler J, Grimm RH Jr, Berge KG, Cohen JD, Lacy CR, Perry HM Jr, Blafox MD, Wassertheil-Smoller S, Black HR, Schron E, Berkson DM, Curb JD, Smith WM, McDonald R, Applegate WB Prevention of heart failure by antihypertensive drug treatment in older persons with isolated systolic hypertension. SHEP Cooperative Research Group. *JAMA* 1997;278:212-6 [[9218667](#)]

Kostis JB, Cabrera J, Cheng JQ, Cosgrove NM, Deng Y, Pressel SL, Davis BR Association between chlorthalidone treatment of systolic hypertension and long-term survival. *JAMA* 2011 Dec 21;306:2588-93 [[22187278](#)] [10.1001/jama.2011.1821](#)

**SHEP (diabetic subgroup), 1996:**

Curb JD, Pressel SL, Cutler JA, Savage PJ, Applegate WB, Black H, Camel G, Davis BR, Frost PH, Gonzalez N, Guthrie G, Oberman A, Rutan GH, Stamler J Effect of diuretic-based antihypertensive treatment on cardiovascular disease risk in older diabetic patients with isolated systolic hypertension. Systolic Hypertension in the Elderly Program Cooperative Research Group. *JAMA* 1996;276:1886-92 [[8968014](#)]

**SHEP-P (subgroup), 1989:**

Perry HM Jr, Smith WM, McDonald RH, Black D, Cutler JA, Furberg CD, Greenlick MR, Kuller LH, Schnaper HW, Schoenberger JA Morbidity and mortality in the Systolic Hypertension in the Elderly Program (SHEP) pilot study. *Stroke* 1989;20:4-13 [[2911834](#)]

**SHEP (subgroup), 1991:**



Prevention of stroke by antihypertensive drug treatment in older persons with isolated systolic hypertension. Final results of the Systolic Hypertension in the Elderly Program (SHEP). SHEP Cooperative Research Group. JAMA 1991;265:3255-64 [2046107]

**DORADO-AC, :**

**DORADO, 2009:**

Weber MA, Black H, Bakris G, Krum H, Linas S, Weiss R, Linseman JV, Wiens BL, Warren MS, Lindholm LH A selective endothelin-receptor antagonist to reduce blood pressure in patients with treatment-resistant hypertension: a randomised, double-blind, placebo-controlled trial. Lancet 2009;374:1423-31 [19748665]

**HSCS, 1974:**

Effect of antihypertensive treatment on stroke recurrence. Hypertension-Stroke Cooperative Study Group. JAMA 1974 Jul 22;229:409-18 [4599980]

Effect of antihypertensive treatment on stroke recurrence. Hypertension-Stroke Cooperative Study Group. JAMA 1974;229:409-18 [4599980]

**USPHS, 1977:**

Smith WM. Treatment of mild hypertension: results of a ten-year intervention trial Circ Res. 1977; 40(5 suppl 1):I98-I105.

Smith WM Treatment of mild hypertension: results of a ten-year intervention trial. Circ Res 1977;40:I98-105 [140029]

**HYRIM, 2005:**

Anderssen SA, Hjelstuen AK, Hjermmann I, Bjerkan K, Holme I Atherosclerosis 2005 Feb;178:387-97 [15694949]

**EWPHE (subgroup ), 1985:**

Amery A, Birkenhger W, Brixko P, Bulpitt C, Clement D, Deruyttere M, De Schaepdryver A, Dollery C, Fagard R, Forette F Mortality and morbidity results from the European Working Party on High Blood Pressure in the Elderly trial. Lancet 1985;1:1349-54 [2861311]

**MRC old, 1992:**

Medical Research Council trial of treatment of hypertension in older adults: principal results. MRC Working Party. BMJ 1992;304:405-12 [1445513]

**Kuramoto, 1981:**

**EWPHE, 1985:**

Amery A, Birkenhager W, Brixko P, Bulpitt C, Clement D, Deruyttere M, De Schaepdryver A, Dollery C, Fagard R, Forette F Mortality and morbidity results from the European Working Party on High Blood Pressure in the Elderly trial. Lancet 1985 Jun 15;1:1349-54 [2861311]

**HYVET, 2008:**

Beckett NS, Peters R, Fletcher AE, Staessen JA, Liu L, Dumitrascu D, Stoyanovsky V, Antikainen RL, Nikitin Y, Anderson C, Belhani A, Forette F, Rajkumar C, Thijs L, Banya W, Bulpitt CJ Treatment of Hypertension in Patients 80 Years of Age or Older. N Engl J Med 2008 Mar 31;: [18378519]

**PATS, 1995:**

Post-stroke antihypertensive treatment study. A preliminary result. PATS Collaborating Group. Chin Med J (Engl) 1995;108:710-7 [8575241]

**IDNT (irbesartan vs pbo), 2001:**

Lewis EJ, Hunsicker LG, Clarke WR, Berl T, Pohl MA, Lewis JB, Ritz E, Atkins RC, Rohde R, Raz I Renoprotective effect of the angiotensin-receptor antagonist irbesartan in patients with nephropathy due to type 2 diabetes. N Engl J Med 2001;345:851-60 [11565517]

Lewis EJ, Hunsicker LG, Clarke WR, Berl T, Pohl MA, Lewis JB, Ritz E, Atkins RC, Rohde R, Raz I Renoprotective effect of the angiotensin-receptor antagonist irbesartan in patients with nephropathy due to type 2 diabetes. N Engl J Med 2001;345:851-60 [11565517]

**IRMA 2, 2001:**

Parving HH, Lehnert H, Brchner-Mortensen J, Gomis R, Andersen S, Arner P The effect of irbesartan on the development of diabetic nephropathy in patients with type 2 diabetes. N Engl J Med 2001;345:870-8 [11565519] 10.1056/NEJMoa011489

**IDNT (irbesartan vs pbo), 2001:**

Lewis EJ, Hunsicker LG, Clarke WR, Berl T, Pohl MA, Lewis JB, Ritz E, Atkins RC, Rohde R, Raz I Renoprotective effect of the angiotensin-receptor antagonist irbesartan in patients with nephropathy due to type 2 diabetes. N Engl J Med 2001;345:851-60 [11565517]

**IPDM (150mg), 2001:**

Parving HH, Lehnert H, Brchner-Mortensen J, Gomis R, Andersen S, Arner P The effect of irbesartan on the development of diabetic nephropathy in patients with type 2 diabetes. N Engl J Med 2001;345:870-8 [11565519]

**RENAAL, 2001:**

Brenner BM, Cooper ME, de Zeeuw D, Keane WF, Mitch WE, Parving HH, Remuzzi G, Snapinn SM, Zhang Z, Shahinfar S Effects of losartan on renal and cardiovascular outcomes in patients with type 2 diabetes and nephropathy. N Engl J Med 2001;345:861-9 [11565518]



**RENAAL, 2001:**

Brenner BM, Cooper ME, de Zeeuw D, Keane WF, Mitch WE, Parving HH, Remuzzi G, Snapinn SM, Zhang Z, Shahinfar S Effects of losartan on renal and cardiovascular outcomes in patients with type 2 diabetes and nephropathy. *N Engl J Med* 2001;345:861-9 [[11565518](#)]

**PROPELLS, 2008:**

Yusuf S, Diener HC, Sacco RL, Cotton D, Ounpuu S, Lawton WA, Palesch Y, Martin RH, Albers GW, Bath P, Bornstein N, Chan BP, Chen ST, Cunha L, Dahlf B, De Keyser J, Donnan GA, Estol C, Gorelick P, Gu V, Hermansson K, Hilbrich L, Kaste M, Lu C, Machnig T, — *N Engl J Med* 2008;359:1225-37 [[18753639](#)]  
[10.1056/NEJMoa0804593](#)

**Cice et al, 2006:****7 heart failure**

Trial	Treatments	Patients	Trials design and methods
<b>Mesenchymal stem cells vs allogeneic mesenchymal stem cells</b>			
<a href="#">POSEIDON, 2012</a> [NCT01087996] n=NA follow-up:	allogeneic MSCs versus autologous bone marrowderived mesenchymal stem cells delivered by transendocardial injection	patients with LV dysfunction due to ICM	
<b>amlodipine vs control</b>			
<a href="#">Packer, 1991</a> <i>unpublished</i> n=NA follow-up: 2 months	-	CHD multiple cause, NYHA class II-III	Double blind
<a href="#">Smith, 1994</a> n=NA follow-up: 3 months	-	CHD multiple cause, NYHA class II-III	Double blind
<a href="#">Binkley, 1996</a> <i>unpublished</i> n=NA follow-up: 3 months	-	CHD multiple cause, NYHA class II-III	Double blind
<a href="#">Udelson, 1996</a> <i>unpublished</i> n=NA follow-up: 3 months	-	patients with congestive heart failure due to ischaemic heart disease, NYHA class II-III	Double blind
<a href="#">Ghali, 1997</a> <i>unpublished</i> n=NA follow-up: 3 months	-	CHD multiple cause, NYHA class III-IV	Double blind
<b>atorvastatin vs control</b>			
<a href="#">Wojnicz, 2006</a> n=36/38 follow-up: 6 months	atorvastatin 40 mg/day versus conventional treatment for heart failure	patients with inflammatory dilated cardiomyopathy (DC) (positive immunohistochemistry results on endomyocardial biopsy)	Parallel groups open
<a href="#">Yamada, 2007</a> n=19/19 follow-up: mean 2.58y	atorvastatin 10 mg/d versus standard treatment	outpatients with mild to moderate CHF and radionuclide left ventricular ejection fraction (LVEF) <40%	Parallel groups

continued...

Trial	Treatments	Patients	Trials design and methods
<b>benazepril vs control</b>			
McGany , 1991 <i>unpublished</i> n=29/32 follow-up:	-	-	
<b>BNP-guided management vs control</b>			
TIME CHF , 2009 n=251/248 follow-up:	intensive BNP-guided therapy versus standard symptom-guided therapy	patients with heart failure, with the specific inclusion of patients & iexcl;& Yacute;75 years of age	Parallel groups open
PRIMA n=174/171 follow-up: 702 days	NT-proBNP guided management versus clinically guided management	Patients admitted for worsening heart failure and with NT-proBNP decreasing during their admission	Parallel groups open the Netherlands
PROTECT , 2009 [NCT00351390] n=NA follow-up:	natriuretic-peptide-guided therapy versus standard management	patients with NYHA class 2-4 heart failure, LVEF <40% , and history of at least one admission or outpatient diuretic dose increase for heart-failure destabilization in the previous six months	Parallel groups
STARS-BNP , 2007 n=110/110 follow-up: 6 mo	BNP-guidance as a supplement to clinical judgment versus traditional approach	patients in NYHA functional class 2-3 with an LVEF <45% ; optimally treated with angiotensin-converting enzyme inhibitors (ACEIs), beta-blockers, and diuretics by CHF specialists	Parallel groups open
BATTLESCARRED , 2009 [ANZCTR12605000735651] n=121/122 follow-up: 3y	drug treatment directed by plasma NTproBNP for 2 years versus usual care	patients admitted to hospital for HF	Parallel groups open New Zealand
STARBRITE , 2007 [NCT00484770] n=NA follow-up: 3 mo	BNP-guided treatment versus clinically based management	patients in NYHA class 3-4 and with an LVEF <35% ; enrolled prior to discharge following hospitalization for acute decompensation	Parallel groups open
Troughton , 2000 n=33/36 follow-up: 9.5 mo (>6 mo)	BNP-guided treatment versus empirical trial-based therapy dictated by clinical acumen617Ow	patients with impaired systolic function (leftventricular ejection fraction <40% ) and symptomatic heart failure (New York Heart Association class IIIV); treated with ACE inhibitors, loop diuretic with or without digoxin	Parallel groups open UK
BASEL <i>ongoing</i> [NCT00130611] n=NA follow-up: 3 months	BNP guided diagnostics and initial therapy versus control	patients presenting with acute dyspnea	Parallel groups Open

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
van Kraaij <i>ongoing</i> [NCT00149422] n=NA follow-up:	NT-proBNP guided treatment versus control	chronic congestive heart failure	Parallel groups single blind
RABBIT <i>ongoing</i> [NCT00206856] n=NA follow-up:	-	-	
<b>Bone marrow derived stem cell vs control</b>			
CUPID 2b , 2016 [NCT01643330] n=NA follow-up:	-	patients with advanced heart failure	
FOCUS-CCTRN , 2012 [NCT00824005] n=92 follow-up:	-	patients with chronic ischemic heart failure	
Pokushalov (DOUBLON DIB) , 2010 n=55/54 follow-up:	Intramyocardial transplantation of autologous bone marrow mononuclear cells versus optimal medical therapy	patients with severe ischemic heart failure	Russia
<b>Bone marrow mononuclear cells vs control</b>			
Ang , 2008 n=NA	-	Elective CABG patients with established myocardial scars diagnosed as akinetic or dyskinetic segments by dobutamine stress echocardiography and confirmed at surgery	single-blinded
Hendriks , 2006 n=NA follow-up: 4 months	-	patients with a postinfarction nonviable scar	
TOPCARE-CHD , 2006 [ NCT00289822] n=NA	-	patients with stable ischemic heart disease who had had a myocardial infarction at least 3 months previously	
Yao , 2008 n=24/23	-	patients with stable ischaemic heart disease due to a previous MI	
<b>Bone marrow progenitor cells vs control</b>			
Manginas , 2007 n=NA	-	patients with old, nonviable anterior myocardial infarction	
Patel , 2005 n=10/10	-	patients with ischemic cardiomyopathy and an ejection fraction of less than 35% who were scheduled for primary off-pump coronary artery bypass grafting	

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
Perin , 2012 n=10/10 follow-up: 6 months	-	patients with advanced ischemic heart failure	
Vrtovec , 2011 [NCT00629018] n=NA	-	patients with dilated cardiomyopathy	
Vrtovec , 2013 [NCT01350310] n=55/55	-	patients with dilated cardiomyopathy	
<b>Cardiac stem cells vs control</b>			
SCIPIO , 2011 [NCT00474461] n=NA follow-up:	-	Patients With Ischemic Cardiomyopathy	
<b>Cardiopoietic stem cell vs control</b>			
C CURE , 2013 [NCT00810238] n=NA follow-up:	-	patients with heart failure of ischemic origin	
CADUCEUS , 2012 [NCT00893360] n=17	-	patients with left ventricular dysfunction after myocardial infarction	
<b>enalapril vs control</b>			
Enalapril CHF investigators , 1987 n=126/130 follow-up:	-	-	
Rucinska-a (enalapril) , 1991 <i>unpublished</i> n=67/65 follow-up:	-	-	
Rucinska-b (enalapril) , 1991 <i>unpublished</i> n=55/55 follow-up:	-	-	
<b>Exercise training vs control</b>			
Dubach et al , 1997 n=24/26 follow-up: 0.7 y	Supervised walking, two hours daily; supervised cycling 40minutes four days a week versus control	patients with chronic heart failure	open Switzerland

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
Giannuzzi et al , 1997 n=46/42 follow-up: 0.6 y	Supervised cycling, 30 minutes three days a week for two months, then home based 30 minutes for three days a week and walking for 30 minutes versus control	patients with <40% ejection fraction after a first Q-wave myocardial infarction	open Italy
Belardinelli et al , 1999 n=50/49 follow-up: 3.1 y	Supervised cycling, 60 minutes three days a week for eight weeks, then two days a week versus no exercise	patients with CHF	open 65279;Italy
Hambrecht et al , 1995 n=34/35 follow-up: 0.4 y	Supervised and home based walking, calisthenics, cycling 40-60 minutes a day versus physically inactive control group	patients with chronic heart failure	open Germany
ExTraMATCH , 2004 n=NA follow-up:	-	-	
Kiilavuori et al , 2000 n=12/15 follow-up: 6.3 y	Supervised cycling 30 minutes three days a week for three months, then home based training (walking, cycling, rowing, and swimming) versus control	patients with stable NYHA class II-III CHF	open Finland
McKelvie et al , 2002 n=90/91 follow-up: 1.5 y	Supervised aerobic (cycling, treadmill, arm) and resistance training 30 minutes three days a week for three months, then home based aerobic training three days a week versus usual care	patients in NYHA class I to III, with ejection fraction <40% and 6-minute walk distance <500 meters	single blind Canada
Zanelli et al , 1997 n=76/79 follow-up: 0.8 y	-	-	Italy
Wielenga et al , 1999 n=41/39 follow-up: 3.9 y	Supervised cycling, walking, ball game 30 minutes three days a week for eight weeks, then two days a week versus control	patients with chronic heart failure NYHA II-III	open Netherlands

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>Willenheimer et al , 1998</b> n=22/30 follow-up: 4.4 y	Supervised interval cyclingtraining (90 second exercise and 30 second rest) for 15-45 minutes two days a weekc versus control	patients with stable mild-to-moderate heart failure	open Sweden
<b>hydralazine vs control</b>			
<b>Chatterjee , 1980</b> n=NA follow-up:	oral hydralazine versus NA	patients with chronic CHF	
<b>myoblasts vs control</b>			
<b>CAuSMIC , 2005</b> n=12/11 follow-up: 12 mo	3-dimensional guided catheter-based delivery of autologous skeletal myoblasts versus control	patients with previous myocardial infarction and heart failure, New York Heart Association (NYHA) functional class II to IV	
<b>SEISMIC , 2011</b> n=26/14 follow-up: 6 mo	percutaneous intramyocardial transplantation of autologous skeletal myoblasts versus control	Patientst with heart failure patients with implanted cardioverter-defibrillators	
<b>nicardipine vs control</b>			
<b>Gheorghiad , 1991</b> <i>unpublished</i> n=NA follow-up: 4 months	-	CHD multiple cause, NYHA class III	Double blind
<b>Abrams , 1993</b> <i>unpublished</i> n=NA follow-up: 4 months	-	CHD multiple cause, NYHA class III-IV	Double blind
<b>ramipril vs control</b>			
<b>Swedberg , 1991</b> n=115/108 follow-up:	-	-	
<b>simvastatin vs control</b>			
<b>Hong , 2005</b> n=106/96 follow-up: 1 year	simvastatin versus no treatment	patients with ischemic heart failure who underwent percutaneous coronary intervention (PCI) for acute myocardial infarction (left ventricular [LV] ejection fraction <40% )	Parallel groups open
<b>spironolactone vs control</b>			
<b>Cicoira , 2002</b> n=54/52 follow-up: 12 months	spironolactone 12.5 to 50 mg/day versus control	patients with chronic heart failure	Parallel groups open

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>Cicoira , 2004</b> n=47/46 follow-up: 12 months	spironolactone versus control	chronic heart failure patients	open
<b>Ramires , 2000</b> n=19/16 follow-up: 20 weeks	spironolactone versus standard medical treatment	patients with systolic dysfunction and NYHA class III CHF secondary to dilated or ischemic cardiomyopathy	Parallel groups open
<b>structured exercise training vs control</b>			
<b>Patwala , 2009</b> n=25/25 follow-up: 6 months	program of physician-supervised exercise training versus control	patients with chronic systolic heart failure receiving a Cardiac Resynchronization Therapy device	Parallel groups open
<b>HF-ACTION , 2008</b> [NCT00047437] n=1159/1172 follow-up: mean 2.5 y	highly structured exercise program focused on increasing workout intensity and duration versus usual care,including recommendations for daily exercise	heart-failure patients (NYHA class 2-4, ejection fraction <35% )	Parallel groups open USA, Canada, France
<b>sacubitril/valsartan vs enalapril</b>			
<b>PARADIGM-HF , 2014</b> [NCT01035255] n=NA follow-up:	-	-	-
<b>losartan 150mg vs losartan 50mg</b>			
<b>HEAL , 2009</b> [NCT00090259] n=1921/1913 follow-up: 4.7 y (median)	losartan 150mg daily versus losartan 50 mg daily	patients with systolic heart failure who couldn't tolerate ACE inhibitors	Parallel groups double blind 30 countries
<b>amiodarone vs no treatment</b>			
<b>GESICA , 1994</b> n=260/256 follow-up: 110 years	amiodarone 300 mg/day versus no treatment	patients with severe heart failure Any two of CTR >0.55, LVEF<=35% , echo LVED >32 cm/m2	open
<b>EPAMSA , 1985</b> n=66/61 follow-up: 081 years	amiodarone 400 mg/day versus no treatment	patients with reduced left ventricular ejection fraction ( <35% ) and asymptomatic ventricular arrhythmias (Lown classes 2 and 4) LVEF <=35% and Lown class 25	open
<b>aspirin vs no treatment</b>			
<b>WASH (aspirin) , 2004</b> n=91/99 follow-up: 27 months	aspirin 300 mg/day versus no treatment	patients with heart failure and left ventricular systolic dysfunction requiring diuretic therapy with LVEF<=35%	open UK, US
<b>warfarin vs no treatment</b>			

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>WASH (warfarin) , 2004</b> n=89/99 follow-up: 27 months	warfarin (target INR 2.5) versus no treatment	patients with heart failure and left ventricular systolic dysfunction requiring diuretic therapy with LVEF <=35%	Parallel groups open UK, US
<b>valsartan vs no valsartan</b>			
<b>VALIDD , 2007</b> [NCT00170924] n=186/198 follow-up: 38 weeks	valsartan titrated up to 320 mg once daily versus placebo	Patients with hypertension and evidence of diastolic dysfunction	Parallel groups double blind USA, canada
<b>Aliskiren vs placebo</b>			
<b>ASTRONAUT , 2013</b> [NCT00894387] n=1639 follow-up: 6 months	Aliskiren versus placebo	stable patients with heart failure, an LVEF <40% (mean 28% ), and elevated natriuretic peptides who had been discharged from a heart-failure hospitalization an average of five days before	Parallel groups double blind North and South america, Europe, Asia
<b>amiloride vs placebo</b>			
<b>Cheitlin , 1991</b> n=12/12 follow-up: 12 weeks	amiloride versus placebo	men with a history of congestive heart failure	Cross over double blind
<b>amiodarone vs placebo</b>			
<b>Nicklas , 1991</b> n=101 follow-up: NA	amiodarone 200 mg/day versus placebo	patients with ejection fractions less than 30% , New York Heart Association class III or IV symptoms, and frequent but asymptomatic spontaneous ventricular ectopy (Lown class II to V) LVEF <=30% and Lown class 25	double blind
<b>Hamer , 1989</b> n=34 follow-up: 163 years	amiodarone 200 mg/day versus placebo	patients with severe congestive heart failure but no sustained ventricular arrhythmia	double blind
<b>STATCHF , 1995</b> n=674 follow-up: 215 years	amiodarone 200 mg/day versus placebo	patients with symptoms of congestive heart failure, cardiac enlargement, 10 or more premature ventricular contractions per hour, and a left ventricular ejection fraction of 40 percent or less LVEF <=40% and >=10 VPD/h and LVED >=55 mm or CTR >055	double blind
<b>amlodipine vs placebo</b>			
<b>PRAISE , 1996</b> n=571/582 follow-up: median 13.8 mo (range 6-33 mo)	amlodipine 10 mg once daily versus placebo	patients with severe chronic heart failure and ejection fractions of less than 30 percent appl	Parallel groups Double blind US

continued...



Trial	Treatments	Patients	Trials design and methods
<b>PRAISE II , 2000</b> <i>unpublished</i> n=826/826 follow-up: up to 4 years	Amlodipine versus placebo	heart failure in non ischemic cardiomyopathy	
<b>Amrinone vs placebo</b>			
<b>AMTG , 1985</b> n=NA follow-up: 3 months	Amrinone <600mg/day versus placebo	patients with heart failure NYHA III/IV	Parallel groups double blind

More details and results :

- angiotensin-Converting Enzyme Inhibitors for heart failure in all type of heart failure at <http://www.trialresultscenter.org/go-Q43>
- beta-blockers for heart failure in all type of heart failure at <http://www.trialresultscenter.org/go-Q44>
- antiarrhythmic drugs for heart failure in all type of heart failure at <http://www.trialresultscenter.org/go-Q46>
- angiotensin-receptor blockers for heart failure in all type of patients at <http://www.trialresultscenter.org/go-Q65>
- angiotensin-receptor blockers for heart failure in patients intolerant to ACE inhibitors at <http://www.trialresultscenter.org/go-Q66>
- angiotensin-receptor blockers for heart failure in patients previously untreated with ACE inhibitors at <http://www.trialresultscenter.org/go-Q67>
- angiotensin-receptor blockers for heart failure in patients already receiving ACE inhibitor at <http://www.trialresultscenter.org/go-Q68>
- calcium channel blockers for heart failure in all type of patients at <http://www.trialresultscenter.org/go-Q70>
- angiotensin-Converting Enzyme Inhibitors for heart failure in elderly at <http://www.trialresultscenter.org/go-Q71>
- antithrombotics for heart failure in patients hospitalized for heart failure at <http://www.trialresultscenter.org/go-Q72>
- antithrombotics for heart failure in all type of patients at <http://www.trialresultscenter.org/go-Q73>
- diuretics for heart failure in patients already taking diuretics at <http://www.trialresultscenter.org/go-Q74>
- diuretics for heart failure in all type of patients at <http://www.trialresultscenter.org/go-Q75>
- cholesterol lowering intervention for heart failure in elderly at <http://www.trialresultscenter.org/go-Q77>
- vasodilators therapy for heart failure in all type of patient at <http://www.trialresultscenter.org/go-Q79>
- Exercise Therapy for heart failure in all type of patients at <http://www.trialresultscenter.org/go-Q88>
- resynchronization (CRT) - defibrillators (ICD) for heart failure in all type of patients at <http://www.trialresultscenter.org/go-Q104>
- phosphodiesterase III inhibitors for heart failure in all type of patients at <http://www.trialresultscenter.org/go-Q117>
- beta-blockers for heart failure in elderly patients at <http://www.trialresultscenter.org/go-Q119>
- cholesterol lowering intervention for heart failure in all type of patients at <http://www.trialresultscenter.org/go-Q176>

## References

### POSEIDON, 2012:

Hare JM, Fishman JE, Gerstenblith G, Difede Velazquez DL, Zambrano JP, Suncion VY, Tracy M, Gherlin E, Johnston PV, Brinker JA, Breton E, Davis-Sproul J, Schulman IH, Byrnes J, Mendizabal AM, Lowery MH, Rouy D, Altman P, Wong Po Foo C, Ruiz P, Amador A, D Comparison of Allogeneic vs Autologous Bone Marrow-Derived Mesenchymal Stem Cells Delivered by Transendocardial Injection in Patients With Ischemic Cardiomyopathy: The POSEIDON Randomized Trial. JAMA 2012 Nov 6;;1-11 [23117550] 10.1001/jama.2012.25321

**Packer, 1991:**

unpublished

Packer M, Nicod P, Khanderia RE Randomized, multicenter, double-blind, placebo-controlled evaluation of amlodipine in patients with mild-to-moderate heart failure (abstr). *J Am Coll Cardiol* 1991;17:274A.

**Smith, 1994:**

Udelson JE, DeAbate CA, Berk M, Neuberg G, Packer M, Vijay NK, Gorwitt J, Smith WB, Kukin ML, LeJemtel T, Levine TB, Konstam MA Effects of amlodipine on exercise tolerance, quality of life, and left ventricular function in patients with heart failure from left ventricular systolic dysfunction. *Am Heart J* 2000 Mar;139:503-10 [[10689266](#)]

**Binkley, 1996:**

unpublished

Binkley PF, Nunziata E, Hatton PS, Cody RJ. Dose and circadian dependent autonomic response to vasodilation with amlodipine in congestive heart failure (abstr) *J Am Coll Cardiol* 1996;27:774.

**Udelson, 1996:**

unpublished

Udelson JE, DeAbate CA, Vijay N. Effect of amlodipine on exercise tolerance and quality of life in mild to moderate heart failure with systolic dysfunction (abstr). *J Am Coll Cardiol* 1996;27:774.

**Ghali, 1997:**

unpublished

Ghali JK, Pressler M, Nye R, Cropp A. Is suppression of the neurohormonal system a prerequisite to improve survival in patients with heart failure and impaired left ventricular systolic function (abstr). *Circulation* 1997;95:385.

**Wojnicz, 2006:**

Wojnicz R, Wilczek K, Nowalany-Kozielska E, Szygula-Jurkiewicz B, Nowak J, Polonski L, Dyrbus K, Badzinski A, Mercik G, Zembala M, Wodniecki J, Rozek MM Usefulness of atorvastatin in patients with heart failure due to inflammatory dilated cardiomyopathy and elevated cholesterol levels. *Am J Cardiol* 2006;97:899-904 [[16516598](#)]

**Yamada, 2007:**

Yamada T, Node K, Mine T, Morita T, Kioka H, Tsukamoto Y, Tamaki S, Masuda M, Okuda K, Fukunami M Long-term effect of atorvastatin on neurohumoral activation and cardiac function in patients with chronic heart failure: a prospective randomized controlled study. *Am Heart J* 2007;153:1055.e1-8 [[17540209](#)]

**McGarry, 1991:**

unpublished

McGarry R. Randomized, Double Blind, Multicenter Study Comparing Benazepril to Digoxin and to Placebo as Add On Therapy to Diuretic in Patients With CHF, NYHA Class II-III During a 12-Week Treatment Period, GHBA-1H. Summit, NJ: Ciba-Geigy Pharmaceuticals; September 1991. Unpublished report.

**TIME CHF, 2009:**

Pfisterer M, Buser P, Rickli H, Gutmann M, Erne P, Rickenbacher P, Vuillomenet A, Jeker U, Dubach P, Beer H, Yoon SI, Suter T, Osterhues HH, Schieber MM, Hilti P, Schindler R, Brunner-La Rocca HP *JAMA* 2009 Jan 28;301:383-92 [[19176440](#)] [10.1001/jama.2009.2](#)

**PRIMA, 0:**

Luc Eurlings Can Pro-Brain Natriuretic Peptide Guided Therapy of Heart Failure Improve Heart Failure Morbidity and Mortality? Main Outcome of the PRIMA-Study ACC.09/i2, Orlando, FL, March 2009 [0]

Eurlings LW, van Pol PE, Kok WE, van Wijk S, Lodewijks-van der Bolt C, Balk AH, Lok DJ, Crijs HJ, van Kraaij DJ, de Jonge N, Meeder JG, Prins M, Pinto YM Management of chronic heart failure guided by individual N-terminal pro-B-type natriuretic peptide targets: results of the PRIMA (Can PRO-brain-natriuretic peptide guided therapy of chronic heart failure IMPROVE heart failure morbidity and mortality?) study. *J Am Coll Cardiol* 2010;56:2090-100 [[21144969](#)] [10.1016/j.jacc.2010.07.030](#)

**PROTECT, 2009:****STARS-BNP, 2007:**

Jourdain P, Jondeau G, Funck F, Gueffet P, Le Helloco A, Donal E, Aupetit JF, Aumont MC, Galinier M, Eicher JC, Cohen-Solal A, Juilliere Y Plasma brain natriuretic peptide-guided therapy to improve outcome in heart failure: the STARS-BNP Multicenter Study. *J Am Coll Cardiol* 2007;49:1733-9 [[17448376](#)]

**BATTLESCARRED, 2009:**

Lainchbury JG, Troughton RW, Frampton CM, Yandle TG, Hamid A, Nicholls MG, Richards AM NTproBNP-guided drug treatment for chronic heart failure: design and methods in the "BATTLESCARRED" trial. *Eur J Heart Fail* 2006;8:532-8 [[16829189](#)]

Lainchbury JG, Troughton RW, Strangman KM, Frampton CM, Pilbrow A, Yandle TG, Hamid AK, Nicholls MG, Richards AM N-Terminal Pro-B-Type Natriuretic Peptide-Guided Treatment for Chronic Heart Failure Results From the BATTLESCARRED (NT-proBNP-Assisted Treatment To Lessen Serial Cardiac Readmissions and Death) Trial. *J Am Coll Cardiol* 2009 Dec 29;55:53-60 [[20117364](#)]

**STARBRITE, 2007:**

Shah MR, Califf RM, Nohria A, et al. STARBRITE: A randomized pilot trial of BNP-guided therapy in patients with advanced heart failure. [Abstract 2554] American Heart Association Scientific Sessions 2006; November 13, 2007

**Troughton, 2000:**

Troughton RW, Frampton CM, Yandle TG, Espiner EA, Nicholls MG, Richards AM Treatment of heart failure guided by plasma aminoterminal brain natriuretic peptide (N-BNP) concentrations. *Lancet* 2000;355:1126-30 [[10791374](#)]

**BASEL, :**

ongoing trial NCT00130611

**van Kraaij, :**

ongoing trial NCT00149422

**RABBIT, :**

ongoing trial NCT00206856

**CUPID 2b, 2016:**

Greenberg B, Butler J, Felker GM, Ponikowski P, Voors AA, Desai AS, Barnard D, Bouchard A, Jaski B, Lyon AR, Pogoda JM, Rudy JJ, Zsebo KM Calcium upregulation by percutaneous administration of gene therapy in patients with cardiac disease (CUPID 2): a randomised, multinational, double-blind, placebo-controlled, phase 2b trial. *Lancet* 2016;387:1178-86 [[26803443](#)]

**FOCUS-CCTRN, 2012:**

Perin EC, Willerson JT, Pepine CJ, Henry TD, Ellis SG, Zhao DX, Silva GV, Lai D, Thomas JD, Kronenberg MW, Martin AD, Anderson RD, Traverse JH, Penn MS, Anwaruddin S, Hatzopoulos AK, Gee AP, Taylor DA, Cogle CR, Smith D, Westbrook L, Chen J, Handberg E, O Effect of Transendocardial Delivery of Autologous Bone Marrow Mononuclear Cells on Functional Capacity, Left Ventricular Function, and Perfusion in Chronic Heart Failure: The FOCUS-CCTRN Trial. *JAMA* 2012 Mar 24;: [[22447880](#)] [10.1001/jama.2012.418](#)

**Pokushalov (DOUBLON DIB), 2010:**

Pokushalov E, Romanov A, Chernyavsky A, Larionov P, Terekhov I, Artyomenko S, Poveshenko O, Kliver E, Shirokova N, Karaskov A, Dib N Efficiency of intramyocardial injections of autologous bone marrow mononuclear cells in patients with ischemic heart failure: a randomized study. *J Cardiovasc Transl Res* 2010;3:160-8 [[20560030](#)] [10.1007/s12265-009-9123-8](#)

**Ang, 2008:**

Ang KL, Chin D, Leyva F, Foley P, Kubal C, Chalil S, Srinivasan L, Bernhardt L, Stevens S, Shenje LT, Galianes M Randomized, controlled trial of intramuscular or intracoronary injection of autologous bone marrow cells into scarred myocardium during CABG versus CABG alone. *Nat Clin Pract Cardiovasc Med* 2008;5:663-70 [[18711405](#)] [10.1038/npcardio1321](#)

**Hendrikx, 2006:**

Hendrikx M, Hensen K, Clijsters C, Jongen H, Koninckx R, Bijmens E, Ingels M, Jacobs A, Geukens R, Dendale P, Vijgen J, Dilling D, Steels P, Mees U, Rummens JL Recovery of regional but not global contractile function by the direct intramyocardial autologous bone marrow transplantation: results from a randomized controlled clinical trial. *Circulation* 2006;114:I101-7 [[16820557](#)] [10.1161/CIRCULATIONAHA.105.000505](#)

**TOPCARE-CHD, 2006:**

Assmus B, Honold J, Schinger V, Britten MB, Fischer-Rasokat U, Lehmann R, Teupe C, Pistorius K, Martin H, Abolmaali ND, Tonn T, Dimmeler S, Zeiher AM Transcatheter transplantation of progenitor cells after myocardial infarction. *N Engl J Med* 2006;355:1222-32 [[16990385](#)] [10.1056/NEJMoa051779](#)

**Yao, 2008:**

Yao K, Huang R, Qian J, Cui J, Ge L, Li Y, Zhang F, Shi H, Huang D, Zhang S, Sun A, Zou Y, Ge J Administration of intracoronary bone marrow mononuclear cells on chronic myocardial infarction improves diastolic function. *Heart* 2008;94:1147-53 [[18381377](#)] [10.1136/hrt.2007.137919](#)

Yao K, Huang RC, Ge L, Qian JY, Li YL, Xu SK, Zhang F, Zhang YQ, Niu YH, Shi JH, Zhang SH, Fan B, Wang QB, Sun AJ, Zou YZ, Ge JB [Observation on the safety: clinical trail on intracoronary autologous bone marrow mononuclear cells transplantation for acute myocardial infarction]. *Zhonghua Xin Xue Guan Bing Za Zhi* 2006 Jul;34:577-81 [[17081355](#)]

**Manginas, 2007:**

Manginas A, Goussetis E, Koutelou M, Karatasakis G, Peristeri I, Theodorakos A, Leontiadis E, Plessas N, Theodosaki M, Graphakos S, Cokkinos DV Pilot study to evaluate the safety and feasibility of intracoronary CD133(+) and CD133(-) CD34(+) cell therapy in patients with nonviable anterior myocardial infarction. *Catheter Cardiovasc Interv* 2007;69:773-81 [[17394248](#)] [10.1002/ccd.21023](#)

**Patel, 2005:**

Patel AN, Geffner L, Vina RF, Saslavsky J, Urschel HC Jr, Kormos R, Benetti F Surgical treatment for congestive heart failure with autologous adult stem cell transplantation: a prospective randomized study. *J Thorac Cardiovasc Surg* 2005;130:1631-8 [[16308009](#)] [10.1016/j.jtcvs.2005.07.056](#)

**Perin, 2012:**

Perin EC, Silva GV, Zheng Y, Gahremanpour A, Canales J, Patel D, Fernandes MR, Keller LH, Quan X, Coulter SA, Moore WH, Herlihy JP, Willerson JT Randomized, double-blind pilot study of transendocardial injection of autologous aldehyde dehydrogenase-bright stem cells in patients with ischemic heart failure. *Am Heart J* 2012;163:415-21, 421.e1 [[22424012](#)] [10.1016/j.ahj.2011.11.020](#)

**Vrtovec, 2011:**

Vrtovec B, Poglajen G, Sever M, Lezaic L, Domanovic D, Cernelc P, Haddad F, Torre-Amione G Effects of intracoronary stem cell transplantation in patients with dilated cardiomyopathy. *J Card Fail* 2011;17:272-81 [[21440864](#)] [10.1016/j.cardfail.2010.11.007](#)

**Vrtovec, 2013:**

Vrtovec B, Poglajen G, Lezaic L, Sever M, Domanovic D, Cernelc P, Socan A, Schrepfer S, Torre-Amione G, Haddad F, Wu JC Effects of intracoronary CD34+ stem cell transplantation in nonischemic dilated cardiomyopathy patients: 5-year follow-up. *Circ Res* 2013;112:165-73 [[23065358](#)] [10.1161/CIRCRESAHA.112.276519](#)

**SCIPIO, 2011:**

Bolli R, Chugh AR, D'Amario D, Loughran JH, Stoddard MF, Ikram S, Beache GM, Wagner SG, Leri A, Hosoda T, Sanada F, Elmore JB, Goichberg P, Cappetta D, Solankhi NK, Fahsah I, Rokosh DG, Slaughter MS, Kajstura J, Anversa P Cardiac stem cells in patients with ischaemic cardiomyopathy (SCIPIO): initial results of a randomised phase 1 trial. *Lancet* 2011;378:1847-57 [[22088800](#)]

Chugh AR, Beache GM, Loughran JH, Mewton N, Elmore JB, Kajstura J, Pappas P, Tautoles A, Stoddard MF, Lima JA, Slaughter MS, Anversa P, Bolli R Administration of cardiac stem cells in patients with ischemic cardiomyopathy: the SCIPIO trial: surgical aspects and interim analysis of myocardial function and viability by magnetic resonance. *Circulation* 2012;126:S54-64 [[22965994](#)]

**C CURE, 2013:**

Bartunek J, Behfar A, Dolatabadi D, Vanderheyden M, Ostojic M, Dens J, El Nakadi B, Banovic M, Beleslin B, Vrolix M, Legrand V, Vrints C, Vanoverschel Cardiopoietic stem cell therapy in heart failure: the C-CURE (Cardiopoietic stem Cell therapy in heart failURE) multicenter randomized trial with lineage-specified biologics. *J Am Coll Cardiol* 2013;61:2329-38 [[23583246](#)]

Bartunek J, Behfar A, Dolatabadi D, Vanderheyden M, Ostojic M, Dens J, El Nakadi B, Banovic M, Beleslin B, Vrolix M, Legrand V, Vrints C, Vanoverschelde JL, Crespo-Diaz R, Homsey C, Tendera M, Waldman S, Wijns W, Terzic A Cardiopoietic stem cell therapy in heart failure: the C-CURE (Cardiopoietic stem Cell therapy in heart failURE) multicenter randomized trial with lineage-specified biologics. *J Am Coll Cardiol* 2013;61:2329-38 [[23583246](#)]

Mielewicz M, Cole GD, Nowbar AN, Schilling R, Whinnett ZI, Bordachar P, Wilmshurst P, Chambers JC, Olshansky B, Morgan J, Israel C, Sethi AS, van Houwelingen M, Cleland JG, Schmidt G, Francis DP The C-CURE Randomized Clinical Trial (Cardiopoietic stem Cell therapy in heart failURE). *J Am Coll Cardiol* 2013;62:2453 [[24355589](#)]

**CADUCEUS, 2012:**

Makkar RR, Smith RR, Cheng K, Malliaras K, Thomson LE, Berman D, Czer LS, Marbn L, Mendizabal A, Johnston PV, Russell SD, Schuleri KH, Lardo AC, Gerstenblith G, Marbn E Intracoronary cardiosphere-derived cells for heart regeneration after myocardial infarction (CADUCEUS): a prospective, randomised phase 1 trial. *Lancet* 2012;379:895-904 [[22336189](#)] [10.1016/S0140-6736\(12\)60195-0](#)

**Enalapril CHF investigators, 1987:**

Enalapril CHF Investigators Long-term effects of enalapril in patients with congestive heart failure: a multicenter, placebo-controlled trial. *Heart Failure*. 1987;3:102-107

**Rucinska-a (enalapril), 1991:**

unpublished

**Rucinska-b (enalapril), 1991:**

unpublished

**Dubach et al, 1997:**

Dubach P, Myers J, Dziekan G, Goebbels U, Reinhart W, Muller P, Buser P, Stulz P, Vogt P, Ratti R Effect of high intensity exercise training on central hemodynamic responses to exercise in men with reduced left ventricular function. *J Am Coll Cardiol* 1997 Jun;29:1591-8 [[9180124](#)]

**Giannuzzi et al, 1997:**

Giannuzzi P, Temporelli PL, Corra U, Gattone M, Giordano A, Tavazzi L Attenuation of unfavorable remodeling by exercise training in postinfarction patients with left ventricular dysfunction: results of the Exercise in Left Ventricular Dysfunction (ELVD) trial. *Circulation* 1997 Sep 16;96:1790-7 [[9323063](#)]

**Belardinelli et al, 1999:**

Belardinelli R, Georgiou D, Cianci G, Purcaro A Randomized, controlled trial of long-term moderate exercise training in chronic heart failure: effects on functional capacity, quality of life, and clinical outcome. *Circulation* 1999 Mar 9;99:1173-82 [[10069785](#)]

**Hambrecht et al, 1995:**

Hambrecht R, Niebauer J, Fiehn E, Klberer B, Offner B, Hauer K, Riede U, Schlierf G, Kbler W, Schuler G Physical training in patients with stable chronic heart failure: effects on cardiorespiratory fitness and ultrastructural abnormalities of leg muscles. *J Am Coll Cardiol* 1995;25:1239-49 [[7722116](#)]

**ExTraMATCH, 2004:**

**Kiilavuori et al, 2000:**

Kiilavuori K, Naveri H, Salmi T, Harkonen M The effect of physical training on skeletal muscle in patients with chronic heart failure. *Eur J Heart Fail* 2000 Mar;2:53-63 [[10742704](#)]

**McKelvie et al, 2002:**

McKelvie RS, Teo KK, Roberts R, McCartney N, Humen D, Montague T, Hendrican K, Yusuf S Effects of exercise training in patients with heart failure: the Exercise Rehabilitation Trial (EXERT). *Am Heart J* 2002 Jul;144:23-30 [[12094184](#)]

**Zanelli et al, 1997:**

**Wielenga et al, 1999:**

Wielenga RP, Huisveld IA, Bol E, Dunselman PH, Erdman RA, Baselier MR, Mosterd WL Safety and effects of physical training in chronic heart failure. Results of the Chronic Heart Failure and Graded Exercise study (CHANGE) *Eur Heart J* 1999 Jun;20:872-9 [[10329092](#)]

**Willenheimer et al, 1998:**

Willenheimer R, Erhardt L, Cline C, Rydberg E, Israelsson B Exercise training in heart failure improves quality of life and exercise capacity. *Eur Heart J* 1998 May;19:774-81 [[9717012](#)]

**Chatterjee, 1980:**

Chatterjee K, Rouleau JL, Massie BM Hydralazine in chronic CHF. *Acta Med Scand Suppl* 1981;652:99-113 [[6949469](#)]

**CAuSMIC, 2005:**

Dib N, Michler RE, Pagani FD, Wright S, Kereiakes DJ, Lengerich R, Binkley P, Buchele D, Anand I, Swingen C, Di Carli MF, Thomas JD, Jaber WA, Opie SR, Campbell A, McCarthy P, Yeager M, Dilsizian V, Griffith BP, Korn R, Kreuger SK, Ghazoul M, MacLellan WR Safety and feasibility of autologous myoblast transplantation in patients with ischemic cardiomyopathy: four-year follow-up. *Circulation* 2005;112:1748-55 [[16172284](#)] [10.1161/CIRCULATIONAHA.105.547810](#)

Dib N, Dinsmore J, Lababidi Z, White B, Moravec S, Campbell A, Rosenbaum A, Seyedmadani K, Jaber WA, Rizenhour CS, Diethrich E One-year follow-up of feasibility and safety of the first U.S., randomized, controlled study using 3-dimensional guided catheter-based delivery of autologous skeletal myoblasts for ischemic cardiomyopathy (CAuSMIC study). *JACC Cardiovasc Interv* 2009;2:9-16 [[19463392](#)] [10.1016/j.jcin.2008.11.003](#)

**SEISMIC, 2011:**

Duckers HJ, Houtgraaf J, Hehrlein C, Schofer J, Waltenberger J, Gershlick A, Bartunek J, Nienaber C, Macaya C, Peters N, Smits P, Siminiak T, van Mieghem W, Legrand V, Serruys PW Final results of a phase IIa, randomised, open-label trial to evaluate the percutaneous intramyocardial transplantation of autologous skeletal myoblasts in congestive heart failure patients: the SEISMIC trial. *EuroIntervention* 2011;6:805-12 [[21252013](#)] [10.4244/EIJV6I7A139](#)

**Gheorghide, 1991:**

unpublished

Georghiade M, Hall V, Goldberg Ad, Levine TB, Goldstein S. Long term clinical and neurohumoral effects of nicardipine in patients with severe heart failure on maintenance therapy with angiotensin converting enzyme inhibitors (abstr). *J Am Coll Cardiol* 1991;17:274A.

**Abrams, 1993:**

unpublished

Abrams J, Bristow MR, Chiang Y. Double-blind evaluation of the safety and efficacy of nicardipine in patients with advanced chronic heart failure (abstr). *J Am Coll Cardiol* 1993;21:377A.

**Swedberg, 1991:**

Swedberg K, Amtorp O, Gundersen T, Remes J, Nilsson B. Is maximal exercise testing a useful method to evaluate treatment of moderate heart failure? *Circulation*. 1991;57:226. Abstract

**Hong, 2005:**

Hong YJ, Jeong MH, Hyun DW, Hur SH, Kim KB, Kim W, Lim SY, Lee SH, Hong SN, Kang DG, Yun KH, Kim KH, Lee YS, Park HW, Kim JH, Ahn YK, Cho JG, Park JC, Kang JC Prognostic significance of simvastatin therapy in patients with ischemic heart failure who underwent percutaneous coronary intervention for acute myocardial infarction. *Am J Cardiol* 2005;95:619-22 [[15721103](#)]

**Cicoira, 2002:**

Cicoira M, Zanolla L, Rossi A, Golia G, Franceschini L, Brighetti G, Marino P, Zardini P, Long-term, dose-dependent effects of spironolactone on left ventricular function and exercise tolerance in patients with chronic heart failure. *J Am Coll Cardiol* 2002;40:304-10. [[12106936](#)]

**Cicoira, 2004:**

Cicoira M, Rossi A, Bonapace S, Zanolla L, Perrot A, Francis DP, Golia G, Franceschini L, Osterziel KJ, Zardini P, Effects of ACE gene insertion/deletion polymorphism on response to spironolactone in patients with chronic heart failure. *Am J Med* 2004;116:657-61. [[15121491](#)] [10.1016/j.amjmed.2003.12.033](#)

**Ramires, 2000:**

Ramires FJ, Mansur A, Coelho O, Maranhão M, Gruppi CJ, Mady C, Ramires JA, Effect of spironolactone on ventricular arrhythmias in congestive heart failure secondary to idiopathic dilated or to ischemic cardiomyopathy. *Am J Cardiol* 2000;85:1207-11. [[10802002](#)]

**Patwala, 2009:**

Patwala AY, Woods PR, Sharp L, Goldspink DF, Tan LB, Wright DJ Maximizing patient benefit from cardiac resynchronization therapy with the addition of structured exercise training: a randomized controlled study. *J Am Coll Cardiol* 2009;53:2332-9 [[19539142](#)]

**HF-ACTION, 2008:**

O'Connor CM, Whellan DJ, Lee KL, Keteyian SJ, Cooper LS, Ellis SJ, Leifer ES, Kraus WE, Kitzman DW, Blumenthal JA, Rendall DS, Miller NH, Fleg JL, Schulman KA, McKelvie RS, Zannad F, Pina IL Efficacy and safety of exercise training in patients with chronic heart failure: HF-ACTION randomized controlled trial. *JAMA* 2009 Apr 8;301:1439-50 [[19351941](#)]

Flynn KE, Pina IL, Whellan DJ, Lin L, Blumenthal JA, Ellis SJ, Fine LJ, Howlett JG, Keteyian SJ, Kitzman DW, Kraus WE, Miller NH, Schulman KA, Spertus JA, O'Connor CM, Weinfurt KP Effects of exercise training on health status in patients with chronic heart failure: HF-ACTION randomized controlled trial. *JAMA* 2009 Apr 8;301:1451-9 [[19351942](#)]

**PARADIGM-HF, 2014:**

McMurray JJ, Packer M, Desai AS, Gong J, Lefkowitz MP, Rizkala AR, Rouleau JL, Shi VC, Solomon SD, Swedberg K, Zile MR Angiotensin-Nepriylsin Inhibition versus Enalapril in Heart Failure. *N Engl J Med* 2014 Aug 30;: [[25176015](#)] [10.1056/NEJMoa1409077](#)

**HEAAL, 2009:**

Konstam MA, Poole-Wilson PA, Dickstein K, Drexler H, Justice SJ, Komajda M, Malbecq W, Martinez FA, Neaton JD, Riegger GA, Guptha S *Eur J Heart Fail* 2008;10:899-906 [[18768350](#)]

Konstam MA, Neaton JD, Dickstein K, Drexler H, Komajda M, Martinez FA, Riegger GA, Malbecq W, Smith RD, Guptha S, Poole-Wilson PA Effects of high-dose versus low-dose losartan on clinical outcomes in patients with heart failure (HEAAL study): a randomised, double-blind trial. *Lancet* 2009 Nov 28;374:1840-8 [[19922995](#)] [10.1016/S0140-6736\(09\)61913-9](#)

**GESICA, 1994:**

Doval HC, Nul DR, Grancelli HO, Perrone SV, Bortman GR, Curiel R Randomised trial of low-dose amiodarone in severe congestive heart failure. Grupo de Estudio de la Sobrevida en la Insuficiencia Cardiaca en Argentina (GESICA) *Lancet* 1994;344:493-8 [[7914611](#)]

**EPAMSA, 1985:**



Garguichevich JJ, Ramos JL, Gambarte A, Gentile A, Hauad S, Scapin O, Sirena J, Tibaldi M, Toplikar J Effect of amiodarone therapy on mortality in patients with left ventricular dysfunction and asymptomatic complex ventricular arrhythmias: Argentine Pilot Study of Sudden Death and Amiodarone (EPAMSA). *Am Heart J* 1995;130:494-500 [7661066]

**WASH (aspirin), 2004:**

Cleland JG, Findlay I, Jafri S, Sutton G, Falk R, Bulpitt C, Prentice C, Ford I, Trainer A, Poole-Wilson PA, The Warfarin/Aspirin Study in Heart failure (WASH): a randomized trial comparing antithrombotic strategies for patients with heart failure. *Am Heart J* 2004;148:157-64. [15215806] 10.1016/j.ahj.2004.03.010

**WASH (warfarin), 2004:**

Cleland JG, Findlay I, Jafri S, Sutton G, Falk R, Bulpitt C, Prentice C, Ford I, Trainer A, Poole-Wilson PA, The Warfarin/Aspirin Study in Heart failure (WASH): a randomized trial comparing antithrombotic strategies for patients with heart failure. *Am Heart J* 2004;148:157-64. [15215806] 10.1016/j.ahj.2004.03.010

**VALIDD, 2007:**

American College of Cardiology Annual Scientific Session, New Orleans, LA, March 2007. [0]

Solomon SD, Janardhanan R, Verma A, Bourgoun M, Daley WL, Purkayastha D, Lacourcire Y, Hippler SE, Fields H, Naqvi TZ, Mulvagh SL, Arnold JM, Thomas JD, Zile MR, Aurigemma GP Effect of angiotensin receptor blockade and antihypertensive drugs on diastolic function in patients with hypertension and diastolic dysfunction: a randomised trial. *Lancet* 2007 Jun 23;369:2079-87 [17586303]

**ASTRONAUT, 2013:**

**Cheitlin, 1991:**

Cheitlin MD, Byrd R, Benowitz N, Liu E, Modin G Amiloride improves hemodynamics in patients with chronic congestive heart failure treated with chronic digoxin and diuretics. *Cardiovasc Drugs Ther* 1991;5:719-25 [1888694]

**Nicklas, 1991:**

Nicklas JM, McKenna WJ, Stewart RA, Mickelson JK, Das SK, Schork MA, Krikler SJ, Quain LA, Morady F, Pitt B Prospective, double-blind, placebo-controlled trial of low-dose amiodarone in patients with severe heart failure and asymptomatic frequent ventricular ectopy. *Am Heart J* 1991;122:1016-21 [1927852]

**Hamer, 1989:**

Hamer AW, Arkles LB, Johns JA Beneficial effects of low dose amiodarone in patients with congestive cardiac failure: a placebo-controlled trial. *J Am Coll Cardiol* 1989;14:1768-74 [2685081]

**STATCHF, 1995:**

Singh SN, Fletcher RD, Fisher SG, Singh BN, Lewis HD, Deedwania PC, Massie BM, Colling C, Lazzari D Amiodarone in patients with congestive heart failure and asymptomatic ventricular arrhythmia. *Survival Trial of Antiarrhythmic Therapy in Congestive Heart Failure*. *N Engl J Med* 1995;333:77-82 [7539890]

**PRAISE, 1996:**

Packer M, O'Connor CM, Ghali JK, Pressler ML, Carson PE, Belkin RN, Miller AB, Neuberg GW, Frid D, Wertheimer JH, Cropp AB, DeMets DL Effect of amlodipine on morbidity and mortality in severe chronic heart failure. *Prospective Randomized Amlodipine Survival Evaluation Study Group*. *N Engl J Med* 1996 Oct 10;335:1107-14 [8813041]

**PRAISE II , 2000:**

unpublished

Cabell CH, Trichon BH, Velazquez EJ, Dumesnil JG, Anstrom KJ, Ryan T, Miller AB, Belkin RN, Cropp AB, O'Connor CM, Jollis JG Importance of echocardiography in patients with severe nonischemic heart failure: the second Prospective Randomized Amlodipine Survival Evaluation (PRAISE-2) echocardiographic study. *Am Heart J* 2004;147:151-7 [14691434]

**AMTG, 1985:**

Massie B, Bourassa M, DiBianco R, Hess M, Konstam M, Likoff M, Packer M Long-term oral administration of amrinone for congestive heart failure: lack of efficacy in a multicenter controlled trial. *Circulation* 1985 May;71:963-71 [3886191]

## 8 miscellaneous

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>ARBs vs control</b>			
<b>Suzuki , 2008</b> n=183/183 follow-up:	ARBs (valsartan, candesartan, and losartan) versus no ARBs	patients with diabetes and chronic kidney disease on dialysis	Parallel groups open
<b>candesartan vs control</b>			
<b>Takahashi , 2006</b> n=43/37 follow-up: 19.4 months	candesartan versus control	patients on chronic haemodialysis in stable condition and with no clinical evidence of cardiac disorders	Parallel groups open
<b>candesartan vs conventional treatment</b>			
<b>E-COST , 2005</b> n=1053/995 follow-up:	candesartan, 2 to 12 mg daily versus conventional antihypertensive drugs other than angiotensin converting enzyme inhibitors or ARBs	Japanese essential hypertensive subjects (sitting blood pressure 140-180/90-110 mmHg) aged 35-79 years	Parallel groups single-blind Japan
<b>E-COST-R , 2005</b> n=69/72 follow-up:	candesartan versus conventional treatment	hypertensive subjects 60 to 75 years old with non-diabetic chronic renal insufficiency	Parallel groups open
<b>HIJ-CREATE , 2009</b> n=1024/1025 follow-up: 4.2 y (median)	angiotensin II receptor blocker-based therapy versus non-angiotensin II receptor blocker-based therapy	patients with angiographically documented coronary artery disease and hypertension	Parallel groups open Japan
<b>candesartan vs placebo</b>			
<b>TROPHY , 2006</b> [NCT00227318] n=409/400 follow-up: 4y	candesartan during 2y followed by 2y of placebo versus placebo	subjects with repeated measurements of systolic pressure of 130 to 139 mm Hg and diastolic pressure of 89 mm Hg or lower, or systolic pressure of 139 mm Hg or lower and diastolic pressure of 85 to 89 mm Hg	Parallel groups double-blind USA
<b>SCOPE , 2003</b> n=2477/2460 follow-up: 3.7 y (mean)	candesartan, 816 mg once daily (target 160/90) versus placebo	patients aged 70-89 years, with systolic blood pressure 160-179 mmHg, and/or diastolic blood pressure 90-99 mmHg, and a Mini Mental State Examination (MMSE) test score >24	Parallel groups double-blind 15 countries
<b>irbesartan vs placebo</b>			
<b>IDNT (irbesartan vs pbo) , 2001</b> n=579/569 follow-up: 2.6 y	Irbesartan 300mg/d (target 135/85) versus placebo	hypertensive patients with nephropathy due to type 2 diabetes	Parallel groups double-blind worldwide
<b>IRMA 2 , 2001</b> n=404/207 follow-up: 2 years	irbesartan 150 mg daily or 300 mg daily versus placebo	hypertensive patients with type 2 diabetes and microalbuminuria	Parallel groups double-blind multinational

continued...



<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>losartan vs placebo</b>			
<b>RENAAL , 2001</b> n=751/762 follow-up: 3.4 years	Losartan 50 to 100 mg once daily versus placebo	patients with type 2 diabetes and nephropathy	Parallel groups double-blind
<b>olmesartan vs placebo</b>			
<b>ROADMAP , 2010</b> [NCT00185159] n=2232/2215 follow-up: 3.2 y	olmesartan at 40 mg/day versus placebo	patients with diabetes and at least one additional cardiovascular risk factor, but no evidence of renal dysfunction	Parallel groups double-blind Europe (19 countries)
<b>ORIENT</b> [NCT00141453] n=282/284 follow-up:	olmesartan versus placebo	patients with diabetic Nephropathy and overt proteinuria secondary to type 2 diabetes mellitus	Parallel groups double-blind Japan, Hong Kong
<b>telmisartan vs placebo</b>			
<b>TRANSCEND , 2008</b> [NCT00153101] n=2954/2972 follow-up: median 56 months (IQR 51-64)	telmisartan 80 mg/day versus placebo	high-risk patients intolerant to angiotensin-converting enzyme inhibitors	Parallel groups double blind 40 countries
<b>PROPELLS , 2008</b> [NCT00153062] n=10146/10186 follow-up: 2.5 y	telmisartan 80 mg daily versus placebo	patients who recently had an ischemic stroke	Factorial plan double blind 35 countries
<b>candesartan vs amlodipine</b>			
<b>CASE-J , 2008</b> n=2354/2349 follow-up: 3.2 years	candesartan-based regimen versus amlodipine-based regimen	high-risk Japanese hypertensive patients	Parallel groups open (blinded assessment) Japan
<b>irbesartan vs amlodipine</b>			
<b>IDNT (irbesartan vs amlodipine) , 2001</b> n=579/567 follow-up: 26y	Irbesartan 300mg/d (with a target of 135/85) versus amlodipine 10mg/d (with a target of 135/85)	hypertensive patients with nephropathy due to type 2 diabetes	Parallel groups double-blind worldwide
<b>valsartan vs amlodipine</b>			
<b>VALUE , 2004</b> [NCT00129233] n=7649/7596 follow-up: 4.2 y (mean)	valsartan based regimen versus amlodipine based regimen	patients, aged 50 years or older with treated or untreated hypertension and high risk of cardiac events	Parallel groups Double blind 31 countries
<b>losartan vs atenolol</b>			

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>LIFE , 2002</b> n=4605/4588 follow-up: 4.8 y (mean)	losartan versus atenolol	patients aged 55-80 years, with previously treated or untreated hypertension (sitting blood pressure 160/200/95/115 mm Hg) and ECG signs of LVH.	Parallel groups Double blind USA, Europe
<b>telmisartan vs enalapril</b>			
<b>DETAIL , 2004</b> n=120/130 follow-up: 5 year	telmisartan 80 mg daily versus enalapril 20 mg daily	subjects with type 2 diabetes and early nephropathy	Parallel groups double-blind
<b>candesartan vs hydrochlorothiazide</b>			
<b>ALPINE , 2003</b> n=197/196 follow-up: 1 year	candesartan versus hydrochlorothiazide	newly detected hypertensives	Parallel groups double-blind Sweden
<b>olmesartan 40 mg vs olmesartan 20 mg plus a calcium-channel blocker</b>			
<b>OSCAR , 2011</b> [NCT00134160] n=578/586 follow-up:	high-dose olmesartan 40 mg per day versus 20-mg/day olmesartan comined with standard dose of amlodipine or azelnidipine	high-risk elderly Japanese hypertension patients	Parallel groups Japan
<b>telmisartan vs ramipril</b>			
<b>ONTARGET (telmisartan alone) , 2008</b> [NCT00153101] n=8542/8576 follow-up: 4.7y	telmisartan 80mg daily versus ramipril 10 mg daily	patients patients with coronary, peripheral, or cerebrovascular disease or diabetes with end-organ damage	Parallel groups double blind 40 countries
<b>telmisartan + ramipril vs ramipril</b>			
<b>ONTARGET (association vs ramipril) , 2008</b> [NCT00153101] n=8502/8576 follow-up: 4.7y	telmisartan 80mg + ramipril 10mg daily versus ramipril 10 mg daily	patients patients with coronary, peripheral, or cerebrovascular disease or diabetes with end-organ damage	Parallel groups double blind 40 countries
<b>telmisartan + ramipril vs telmisartan</b>			
<b>ONTARGET (association vs telmisartan) , 2008</b> [NCT00153101] n=8502/8542 follow-up: 4.7y	telmisartan 80mg + ramipril 10mg daily versus telmisartan 80 mg daily	patients patients with coronary, peripheral, or cerebrovascular disease or diabetes with end-organ damage	Parallel groups double blind 40 countries

More details and results :

- angiotensin-receptor blockers for miscellaneous in all type of patients at <http://www.trialresultscenter.org/go-Q425>

## References

**Suzuki, 2008:**

Suzuki H, Kanno Y, Sugahara S, Ikeda N, Shoda J, Takenaka T, Inoue T, Araki R Effect of angiotensin receptor blockers on cardiovascular events in patients undergoing hemodialysis: an open-label randomized controlled trial. *Am J Kidney Dis* 2008;52:501-6 [[18653268](#)] [10.1053/j.ajkd.2008.04.031](#)

#### **Takahashi, 2006:**

Takahashi A, Takase H, Toriyama T, Sugiura T, Kurita Y, Ueda R, Dohi Y Candesartan, an angiotensin II type-1 receptor blocker, reduces cardiovascular events in patients on chronic haemodialysis—a randomized study. *Nephrol Dial Transplant* 2006;21:2507-12 [[16766543](#)] [10.1093/ndt/gfl293](#)

#### **E-COST, 2005:**

Suzuki H, Kanno Y Effects of candesartan on cardiovascular outcomes in Japanese hypertensive patients. *Hypertens Res* 2005;28:307-14 [[16138560](#)] [10.1291/hypres.28.307](#)

#### **E-COST-R, 2005:**

Nakamura T, Kanno Y, Takenaka T, Suzuki H An angiotensin receptor blocker reduces the risk of congestive heart failure in elderly hypertensive patients with renal insufficiency. *Hypertens Res* 2005;28:415-23 [[16156505](#)] [10.1291/hypres.28.415](#)

#### **HIJ-CREATE, 2009:**

Kasanuki H, Hagiwara N, Hosoda S, Sumiyoshi T, Honda T, Haze K, Nagashima M, Yamaguchi J, Origasa H, Urashima M, Ogawa H Angiotensin II receptor blocker-based vs. non-angiotensin II receptor blocker-based therapy in patients with angiographically documented coronary artery disease and hypertension: the Heart Institute of Japan Candesartan Randomized Trial for Evaluation in Coronary Artery Disease (HIJ-CREATE). *Eur Heart J* 2009;30:1203-12 [[19346521](#)] [10.1093/eurheartj/ehp101](#)

#### **TROPHY, 2006:**

Julius S, Nesbitt SD, Egan BM, Weber MA, Michelson EL, Kaciroti N, Black HR, Grimm RH Jr, Messerli FH, Oparil S, Schork MA Feasibility of treating prehypertension with an angiotensin-receptor blocker. *N Engl J Med* 2006;354:1685-97 [[16537662](#)] [10.1056/NEJMoa060838](#)

#### **SCOPE, 2003:**

Saxby BK, Harrington F, Wesnes KA, McKeith IG, Ford GA Candesartan and cognitive decline in older patients with hypertension: a substudy of the SCOPE trial. *Neurology* 2008;70:1858-66 [[18458219](#)] [10.1212/01.wnl.0000311447.85948.78](#)

Lithell H, Hansson L, Skoog I, Elmfeldt D, Hofman A, Olofsson B, Trenkwalder P, Zanchetti A The Study on Cognition and Prognosis in the Elderly (SCOPE): principal results of a randomized double-blind intervention trial. *J Hypertens* 2003;21:875-86 [[12714861](#)] [10.1097/01.hjh.0000059028.82022.89](#)

#### **IDNT (irbesartan vs pbo), 2001:**

Lewis EJ, Hunsicker LG, Clarke WR, Berl T, Pohl MA, Lewis JB, Ritz E, Atkins RC, Rohde R, Raz I Renoprotective effect of the angiotensin-receptor antagonist irbesartan in patients with nephropathy due to type 2 diabetes. *N Engl J Med* 2001;345:851-60 [[11565517](#)]

Lewis EJ, Hunsicker LG, Clarke WR, Berl T, Pohl MA, Lewis JB, Ritz E, Atkins RC, Rohde R, Raz I Renoprotective effect of the angiotensin-receptor antagonist irbesartan in patients with nephropathy due to type 2 diabetes. *N Engl J Med* 2001;345:851-60 [[11565517](#)]

#### **IRMA 2, 2001:**

Parving HH, Lehnert H, Brchner-Mortensen J, Gomis R, Andersen S, Arner P The effect of irbesartan on the development of diabetic nephropathy in patients with type 2 diabetes. *N Engl J Med* 2001;345:870-8 [[11565519](#)] [10.1056/NEJMoa011489](#)

#### **RENAAL, 2001:**

Brenner BM, Cooper ME, de Zeeuw D, Keane WF, Mitch WE, Parving HH, Remuzzi G, Snapinn SM, Zhang Z, Shahinfar S Effects of losartan on renal and cardiovascular outcomes in patients with type 2 diabetes and nephropathy. *N Engl J Med* 2001;345:861-9 [[11565518](#)]

#### **ROADMAP, 2010:**

Ritz E, Viberti GC, Ruilope LM, Rabelink AJ, Izzo JL Jr, Katayama S, Ito S, Mimran A, Menne J, Rump LC, Januszewicz A, Haller H Determinants of urinary albumin excretion within the normal range in patients with type 2 diabetes: the Randomised Olmesartan and Diabetes Microalbuminuria Prevention (ROADMAP) study. *Diabetologia* 2010;53:49-57 [[19876613](#)] [10.1007/s00125-009-1577-3](#)

Haller H, Ito S, Izzo JL Jr, Januszewicz A, Katayama S, Menne J, Mimran A, Rabelink TJ, Ritz E, Ruilope LM, Rump LC, Viberti G Olmesartan for the delay or prevention of microalbuminuria in type 2 diabetes. *N Engl J Med* 2011 Mar 10;364:907-17 [[21388309](#)]

#### **ORIENT, :**

#### **TRANSCEND, 2008:**

#### **PROPHESSE, 2008:**

Yusuf S, Diener HC, Sacco RL, Cotton D, Ounpuu S, Lawton WA, Palesch Y, Martin RH, Albers GW, Bath P, Bornstein N, Chan BP, Chen ST, Cunha L, Dahlf B, De Keyser J, Donnan GA, Estol C, Gorelick P, Gu V, Hermansson K, Hilbrich L, Kaste M, Lu C, Machnig T, — *N Engl J Med* 2008;359:1225-37 [[18753639](#)] [10.1056/NEJMoa0804593](#)

### **CASE-J, 2008:**

Ogihara T, Nakao K, Fukui T, Fukiyama K, Ueshima K, Oba K, Sato T, Saruta T Effects of candesartan compared with amlodipine in hypertensive patients with high cardiovascular risks: candesartan antihypertensive survival evaluation in Japan trial. *Hypertension* 2008 Feb;51:393-8 [[18172059](#)] [10.1161/HYPERTENSION-AHA.107.098475](#)

### **IDNT (irbesartan vs amlodipine), 2001:**

Lewis EJ, Hunsicker LG, Clarke WR, Berl T, Pohl MA, Lewis JB, Ritz E, Atkins RC, Rohde R, Raz I Renoprotective effect of the angiotensin-receptor antagonist irbesartan in patients with nephropathy due to type 2 diabetes. *N Engl J Med* 2001;345:851-60 [[11565517](#)]

### **VALUE, 2004:**

Julius S, Kjeldsen SE, Weber M, Brunner HR, Ekman S, Hansson L, Hua T, Laragh J, McInnes GT, Mitchell L, Plat F, Schork A, Smith B, Zanchetti A Outcomes in hypertensive patients at high cardiovascular risk treated with regimens based on valsartan or amlodipine: the VALUE randomised trial. *Lancet* 2004 Jun 19;363:2022-31 [[15207952](#)]

### **LIFE, 2002:**

Dahlof B, Devereux RB, Kjeldsen SE, Julius S, Beevers G, de Faire U, Fyhrquist F, Ibsen H, Kristiansson K, Lederballe-Pedersen O, Lindholm LH, Nieminen MS, Omvik P, Oparil S, Wedel H Cardiovascular morbidity and mortality in the Losartan Intervention For Endpoint reduction in hypertension study (LIFE): a randomised trial against atenolol. *Lancet* 2002 Mar 23;359:995-1003 [[11937178](#)]

### **DETAIL, 2004:**

Barnett AH, Bain SC, Bouter P, Karlberg B, Madsbad S, Jervell J, Mustonen J Angiotensin-receptor blockade versus converting-enzyme inhibition in type 2 diabetes and nephropathy. *N Engl J Med* 2004;351:1952-61 [[15516696](#)] [10.1056/NEJMoa042274](#)

### **ALPINE, 2003:**

Lindholm LH, Persson M, Alaupovic P, Carlberg B, Svensson A, Samuelsson O Metabolic outcome during 1 year in newly detected hypertensives: results of the Antihypertensive Treatment and Lipid Profile in a North of Sweden Efficacy Evaluation (ALPINE study). *J Hypertens* 2003;21:1563-74 [[12872052](#)] [10.1097/01.hjh.0000084723.53355.76](#)

### **OSCAR, 2011:**

Ogawa H, Kim-Mitsuyama S, Jinnouchi T, Matsui K, Arakawa K Rationale, design and patient baseline characteristics of OlmeSartan and calcium antagonists randomized (OSCAR) study: a study comparing the incidence of cardiovascular events between high-dose angiotensin II receptor blocker (ARB) monotherapy and combination therapy of ARB with calcium channel blocker in Japanese elderly high-risk hypertensive patients (ClinicalTrials.gov no. NCT00134160). *Hypertens Res* 2009;32:575-80 [[19444280](#)] [10.1038/hr.2009.60](#)

### **ONTARGET (telmisartan alone), 2008:**

Yusuf S, Teo KK, Pogue J, Dyal L, Copland I, Schumacher H, Dagenais G, Sleight P, Anderson C Telmisartan, ramipril, or both in patients at high risk for vascular events. *N Engl J Med* 2008 Apr 10;358:1547-59 [[18378520](#)] [10.1056/NEJMoa0801317](#)

Verdecchia P, Sleight P, Mancia G, Fagard R, Trimarco B, Schmieder RE, Kim JH, Jennings G, Jansky P, Chen JH, Liu L, Gao P, Probstfield J, Teo K, Yusuf S Effects of telmisartan, ramipril, and their combination on left ventricular hypertrophy in individuals at high vascular risk in the Ongoing Telmisartan Alone and in Combination With Ramipril Global End Point Trial and the Telmisartan Randomized Assessment Study in ACE Intolerant Subjects With Cardiovascular Disease. *Circulation* 2009;120:1380-9 [[19770395](#)]

### **ONTARGET (association vs ramipril), 2008:**

Yusuf S, Teo KK, Pogue J, Dyal L, Copland I, Schumacher H, Dagenais G, Sleight P, Anderson C Telmisartan, ramipril, or both in patients at high risk for vascular events. *N Engl J Med* 2008 Apr 10;358:1547-59 [[18378520](#)]

### **ONTARGET (association vs telmisartan), 2008:**

Yusuf S, Teo KK, Pogue J, Dyal L, Copland I, Schumacher H, Dagenais G, Sleight P, Anderson C Telmisartan, ramipril, or both in patients at high risk for vascular events. *N Engl J Med* 2008 Apr 10;358:1547-59 [[18378520](#)]

## **9 atrial fibrillation**

Trial	Treatments	Patients	Trials design and methods
<b>losartan vs atenolol</b>			
LIFE (AF ancillary study) , 2005 n=4298/4182 follow-up: 4.8 y	losartan versus atenolol	hypertension	
<b>aspirin vs control</b>			
Japanese AF Trial , 2006 n=426/445 follow-up:	aspirin at 150 to 200 mg per day versus no antiplatelet or anticoagulant therapy	patients with nonvalvular atrial fibrillation	
LASAF(aspirin vs no treatment) , 1999 n=NA follow-up:	aspirin:125mg/day(group A1);125mg on alternate days(group A2) versus no control treatment(group C)	-	Open
<b>atorvastatin vs control</b>			
Ozaydin , 2006 n=24/24 follow-up: 3 months	atorvastatin 10 mg versus standard therapy	Persistent AF and scheduled EC	open
<b>enalapril vs control</b>			
Ueng , 2003 n=70/75 follow-up: 270 days (range 61-575d)	enalapril versus control	atrial fibrillation	Parallel groups open
<b>irbesartan vs control</b>			
Madrid , 2002 n=79/75 follow-up: 254 d (range 60-710)	irbesartan versus control	atrial fibrillation	Parallel groups open
<b>pravastatin vs control</b>			
Tveit , 2004 n=51/51 follow-up: 65279;6 weeks	pravastatin65279; 40 mg versus standard therapy	65279;AF >48 h and scheduled EC	
<b>warfarin low dose vs control</b>			
BAATAF (warfarin vs no treatment) , 1990 [NCT00000517] n=212/208 follow-up: 2.2 years	warfarin low dose (target INR:1.5-2.7) versus no placebo.people received no treatment but could choose to take aspirin.	non rheumatic AF	Parallel groups Open
<b>warfarin low dose + aspirin vs control</b>			
SAFT(warfarin low dose + aspirin vs no treatment) , 2003 n=334/334 follow-up: 33 months	warfarin low dose (1.25 mg/d) + aspirin 75 mg/d versus no treatment	Low-medium risk patients with non valvular atrial fibrillation.	Parallel groups Open Sweden

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>warfarin standard dose vs control</b>			
AFASAK (warfarin standard dose vs control) , 1989 n=335/336 follow-up: 2 years	warfarin standard dose(target INR:2.8-4.2) versus control	chronic non rheumatic AF	Parallel groups Open Denmark
SPAF (warfarin standard dose) , 1991 n=210/211 follow-up: 1.3 years	warfarin standard dose(target INR:2.0-4.5) versus control	-	Parallel groups Open USA
<b>flecainide vs no treatment</b>			
Van Gelder , 1989 n=36/37 follow-up: 12 months	Flecainide 200-300 mg/d versus no treatment	Any persistent AF or AFL	Parallel groups open
<b>amiodarone vs placebo</b>			
Channer , 2004 n=61/38 follow-up: 12 months	Amiodarone 200 mg/d versus placebo	patients with Persistent AF	Parallel groups double blind
GEFACA , 2001 n=35/15 follow-up: 16 months	Amiodarone 200 mg/d versus placebo	Persistent AF lasting >2 months	Parallel groups double blind
Kochiadakis (amiodarone vs placebo) , 2000 n=65/60 follow-up: 24 months	Amiodarone 200 mg/d versus placebo	Any documented symptomatic previous or persistent AF	Parallel groups single
SAFE-T (amiodarone vs placebo) , 2005 n=267/137 follow-up: 12 months	Amiodarone 300 mg/d versus placebo	Persistent AF lasting 3 days to 1 year	Parallel groups double blind
<b>aprimidine vs placebo</b>			
SMART , 2002 n=47/47 follow-up: 6 months	Aprimidine 40 mg/d versus placebo	Symptomatic paroxysmal AF having >1 episode monthly or persistent AF lasting <1 month	Parallel groups double blind
<b>aspirin vs placebo</b>			
EAFIT , 1993 n=404/378 follow-up: 2.3 years	aspirin 300 mg/d versus placebo	Patient with non rheumatic AF and recent TIA or minor ischaemic stroke(secondary prevention).	Parallel groups Double blind europe,israel
AFASAK (aspirin vs placebo) , 1989 n=336/336 follow-up: 2 years	aspirin 75 mg/d versus placebo	patients with chronic non-rheumatic atrial fibrillation	Parallel groups Double aveugle Denmark

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>SPAF (aspirin , warfarin eligible arm) , 1991</b> n=206/211 follow-up: 1.3 years	aspirin 325mg/d versus placebo	nonrheumatic atrial fibrillation, warfarin eligible patients	Parallel groups Double blind USA
<b>SPAF (aspirin, warfarin ineligible arm) , 1991</b> n=346/357 follow-up: 1.3 years	aspirin 325mg/d versus placebo	nonrheumatic atrial fibrillation, warfarin ineligible patients	Parallel groups Double blind USA
<b>Azimilide vs placebo</b>			
<b>ASAP , 2003</b> n=891/489 follow-up: 6 months	Azimilide various doses (35 to 125 mg/d) after pharmacological or electrical cardioversion versus placebo	patients with previous AF documented in the last 2 years	Parallel groups double blind
<b>candesartan vs placebo</b>			
<b>CAPRAF (Tveit) , 2007</b> [NCT00130975] n=86/85 follow-up: 6 months	candesartan 8 mg once daily for 3-6 weeks before and candesartan 16 mg once daily for 6 months after electrical cardioversion versus placebo	patients undergoing electrical cardioversion for persistent AF	Parallel groups double blind
<b>CHARM (AF ancillary study) , 2005</b> n=3225/3221 follow-up: 3.17 y	candesartan versus placebo	Heart failure	
<b>disopyramide vs placebo</b>			
<b>Karlon , 1998</b> n=46/46 follow-up: 12 months	Disopyramide 500 mg/d versus palcebo	Persistent AF between 6 weeks and 1 year	Parallel groups open
<b>Lloyd (Disopyramide vs placebo) , 1984</b> n=29/25 follow-up: 6 months	Disopyramide 450 mg/d , versus placebo	Persistent AF lasting 1 month to 3 years	Parallel groups double blind
<b>dronedarone vs placebo</b>			
<b>PALLAS , 2011</b> [NCT01151137] n=1577/1572 follow-up: 3 years	Dronedarone versus placebo	patients with permanent atrial fibrillation and additional risk factors	Parallel groups double-blind
<b>ADONIS , 2007</b> [NCT00259376] n=417/208 follow-up: 12 months	dronedarone 400 mg twice daily versus placebo	patients with at least one episode of atrial fibrillation in the preceding 3 months, and in sinus rhythm for at least 1 hour before randomization	Parallel groups double blind United States, Canada, Australia, South Africa, Argentina

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>ATHENA , 2009</b> [NCT00174785] n=2301/2327 follow-up: 21.5 months	dronedarone 400 mg twice a day versus placebo	patients (>70y) with paroxysmal or persistent atrial fibrillation and additional risk factors for death	Parallel groups double blind 37 countries
<b>DAFNE , 2003</b> n=151/48 follow-up:	Dronedarone various doses (800, 1200, 1600 mg/d) versus placebo	patients with Persistent AF	Parallel groups double blind
<b>ERATO , 2008</b> [18760136] n=85/89 follow-up: 6 months	dronedarone 400 mg twice daily versus placebo	patients with permanent AF	Parallel groups double blind
<b>EURIDIS , 2007</b> [NCT00259428] n=411/201 follow-up: 12 months	dronedarone 400 mg twice daily versus placebo	patients with at least one episode of atrial fibrillation in the preceding 3 months, and in sinus rhythm for at least 1 hour before randomization	Parallel groups double blind 12 European countries
<b>EURIDIS ADONIS (pooled analysis) , 2009</b> n=828/409 follow-up: 12 months	Dronedarone 800 mg/d versus placebo	AF documented in the previous 3 months	Parallel groups double blind Europe, US, Canada, Australia, South A, Argentina
<b>enalapril vs placebo</b>			
<b>SOLVD (AF ancillary study) , 2003</b> n=186/188 follow-up: 2.9 y	enalapril versus placebo	Heart failure	
<b>flecainide vs placebo</b>			
<b>Carunchio (flecainide vs placebo) , 1995</b> n=20/26 follow-up: 12 months	Flecainide 200 mg/d versus placebo	patients with recurrent AF with >3 episodes in previous 1 year	Parallel groups open
<b>irbesartan vs placebo</b>			
<b>ACTIVE I , 2009</b> [NCT00249795] n=4518/4498 follow-up: 4.1 years	irbesartan 300mg once daily versus placebo	patients with atrial fibrillation and with a systolic blood pressure of at least 110 mmHg associated with at least one major risk of vascular events	Factorial plan double blind
<b>n-3 PUFA vs placebo</b>			
<b>P-OM3 (Kowey) , 2010</b> n=663 follow-up:	omega-3 PUFA capsules at 8 g/day for the first seven days followed by 4 g/day for total of 24 weeks versus placebo	outpatients with documented symptomatic paroxysmal or persistent AF without significant structural heart disease and initially in sinus rhythm	Parallel groups double-blind

continued...



<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>oral anticoagulant vs placebo</b>			
<b>EAF<sup>T</sup> , 1993</b> n=225/214 follow-up: 2.3 years	Oral anticoagulation standard dose(target INR 3.0 (2.5-4.0)) the choice of anticoagulant type was free but most physicians choose coumarin derivatives. versus placebo	Patient with non rheumatic AF and recent TIA or minor ischaemic stroke(secondary prevention).	Parallel groups Open
<b>pilsicainide vs placebo</b>			
<b>Okishige , 2000</b> n=52/10 follow-up:	Pilsicainide 150 mg/d/d versus placebo	Persistent AF lasting >6 months	Parallel groups single
<b>propafenone vs placebo</b>			
<b>Bellandi (propafenone vs placebo) , 2001</b> n=102/92 follow-up: 12 months	Propafenone 900 mg/d/d after pharmacological or electrical cardioversion versus placebo	patients with paroxysmal recurrent or persistent AF	Parallel groups double blind
<b>Dogan , 2004</b> n=58/52 follow-up: 15 months	Propafenone 450 mg/d versus placebo	AF of duration 3 hours to 3 months ???	Parallel groups single
<b>Kochiadakis b (propafenone vs placebo) , 2004</b> n=86/83 follow-up: 24 months	Propafenone 450 mg/d versus placebo	Any documented symptomatic previous or persistent AF	Parallel groups single
<b>RAFT , 2003</b> n=397/126 follow-up: 9 months	Propafenone at various doses (450, 650, 850 mg/d) versus placebo.	Previous symptomatic AF documented in the last year	Parallel groups double blind
<b>Stroobandt , 1997</b> n=77/25 follow-up: 6 months	Propafenone 450 mg/d versus placebo	Recent-onset AF or persistent AF lasting >2 weeks	Parallel groups double blind
<b>rosuvastatin vs placebo</b>			
<b>GISSI HF (subgroup and ancillary study) , 2009</b> [NCT00336336] n=1855/1835 follow-up: 3.7y (median)	rosuvastatin 10mg daily versus placebo	patients with chronic heart failure who were not in AF at study entry	Factorial plan double-blind Italy
<b>sotalol vs placebo</b>			
<b>Bellandi (sotalol vs placebo) , 2001</b> n=106/92 follow-up: 12 months	sotalol 240 mg/d versus placebo	patients with paroxysmal recurrent or persistent AF	Parallel groups double blind

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>Benditt , 1999</b> n=184/69 follow-up: 12 months	Sotalol various doses (80, 120, 160 mg/d) after cardioversion versus placebo	patients with AF or AF <sub>I</sub> documented in the last 3 months	Parallel groups double blind
<b>Carunchio (sotalol vs placebo) , 1995</b> n=20/26 follow-up: 12 months	sotalol 240 mg/d , versus placebo	patients with recurrent AF with >3 episodes in previous 1 year	Parallel groups open
<b>Kochiadakis (sotalol vs placebo) , 2000</b> n=NA follow-up: 24 months	sotalol 320 mg/d versus placebo	Any documented symptomatic previous or persistent AF	Parallel groups single
<b>Kochiadakis b (sotalol vs placebo) , 2004</b> n=85/83 follow-up: 24 months	sotalol 300 mg/d versus placebo	Any documented symptomatic previous or persistent AF	Parallel groups single
<b>PAFAC (sotalol vs placebo) , 2004</b> n=383/88 follow-up: 12 months	sotalol 320 mg/d , versus placebo	Persistent AF lasting >7 daysil	Parallel groups double blind
<b>SAFE-T (sotalol vs placebo) , 2005</b> n=261/132 follow-up: 12 months	sotalol 320 mg/d versus placebo	Persistent AF lasting 3 days to 1 year	Parallel groups double blind
<b>Singh , 1991</b> n=24/10 follow-up: 6 months	Sotalol 80 - 320 mg/d versus placebo	Persistent AF or AF <sub>I</sub> lasting 2 weeks to 1 year	Parallel groups double blind
<b>SOPAT (sotalol vs placebo) , 2004</b> n=264/251 follow-up: 12 months	sotalol 320 mg/d , versus placebo	Paroxysmal AF documented in the last 1 month@4	Parallel groups double blind
<b>trandolapril vs placebo</b>			
<b>TRACE (AF ancillary study) , 1999</b> n=790/787 follow-up: 2.4 y	trandolapil versus placebo	Postmyocardial infarction	
<b>valsartan vs placebo</b>			
<b>Val-HeFT (AF ancillary study) , 2003</b> n=2506/2494 follow-up: 1.92 y	valsartan versus placebo	Heart failure	

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
GISSI-AF (Disertori) , 2009 [NCT00376272] n=722/720 follow-up: 1 year	valsartan versus placebo	patients in sinus rhythm but with either two or more documented episodes of atrial fibrillation in the previous 6 months or successful cardioversion for atrial fibrillation in the previous 2 weeks and with underlying cardiovascular disease, diabetes, or left atrial enlargement	Parallel groups double blind
<b>warfarin low dose vs placebo</b>			
SPINAF (warfarin vs placebo) , 1992 n=260/265 follow-up: 1.75 years	warfarin low dose(target INR 1.4-2.8) versus placebo	men ,with chronic nonrheumatic atrial fibrillation	Parallel groups Double blind usa
<b>warfarin standard dose vs placebo</b>			
CAFA , 1991 n=187/191 follow-up: 15.2 months	warfarin standard dose (target INR 2-3) versus placebo	non rheumatic atrial fibrillation	Parallel groups Double blind canada

More details and results :

- antithrombotics for atrial fibrillation in primary prevention of thromboembolic events at <http://www.trialresultscenter.org/go-Q57>
- rhythm control for atrial fibrillation in all type of patients at <http://www.trialresultscenter.org/go-Q112>
- antiarrhythmic drugs for atrial fibrillation in maintaining sinus rhythm after cardioversion at <http://www.trialresultscenter.org/go-Q113>
- antiarrhythmic drugs for atrial fibrillation in rate control at <http://www.trialresultscenter.org/go-Q273>
- catheter ablation for atrial fibrillation in all type of patients at <http://www.trialresultscenter.org/go-Q320>
- prevention for atrial fibrillation in patient with history of atrial fibrillation at <http://www.trialresultscenter.org/go-Q328>
- prevention for atrial fibrillation in patients without history of AF (primary prevention) at <http://www.trialresultscenter.org/go-Q331>
- embolic protection for atrial fibrillation in all type of patients at <http://www.trialresultscenter.org/go-Q337>
- direct antithrombins for atrial fibrillation in all type of patients at <http://www.trialresultscenter.org/go-Q368>
- direct factor Xa inhibitors for atrial fibrillation in all type of patients at <http://www.trialresultscenter.org/go-Q373>
- direct oral anticoagulant (DAO) for atrial fibrillation in all type of patients at <http://www.trialresultscenter.org/go-Q391>
- antithrombotics for atrial fibrillation in secondary prevention of thromboembolic events at <http://www.trialresultscenter.org/go-Q392>
- rate control for atrial fibrillation in all type of patients at <http://www.trialresultscenter.org/go-Q400>
- antiarrhythmic drugs for atrial fibrillation in prevention of cardiovascular events at <http://www.trialresultscenter.org/go-Q514>
- antithrombotics for atrial fibrillation in patients ineligible for warfarin at <http://www.trialresultscenter.org/go-Q565>

## References

### **LIFE (AF ancillary study), 2005:**

Wachtell K, Lehto M, Gerdtts E, Olsen MH, Hornestam B, Dahlf B, Ibsen H, Julius S, Kjeldsen SE, Lindholm LH, Nieminen MS, Devereux RB Angiotensin II receptor blockade reduces new-onset atrial fibrillation and subsequent stroke compared to atenolol: the Losartan Intervention For End Point Reduction in Hypertension (LIFE) study. *J Am Coll Cardiol* 2005;45:712-9 [[15734615](#)] [10.1016/j.jacc.2004.10.068](#)

### **Japanese AF Trial, 2006:**

Sato H, Ishikawa K, Kitabatake A, Ogawa S, Maruyama Y, Yokota Y, Fukuyama T, Doi Y, Mochizuki S, Izumi T, Takekoshi N, Yoshida K, Hiramori K, Origasa H, Uchiyama S, Matsumoto M, Yamaguchi T, Hori M Low-dose aspirin for prevention of stroke in low-risk patients with atrial fibrillation: Japan Atrial Fibrillation Stroke Trial. *Stroke* 2006 Feb;37:447-51 [[16385088](#)] [10.1161/01.STR.0000198839.61112.ee](#)

### **LASAF(aspirin vs no treatment), 1999:**

Posada IS, Barriales V Alternate-day dosing of aspirin in atrial fibrillation. LASAF Pilot Study Group. *Am Heart J* 1999 Jul;138:137-43 [[10385777](#)]

### **Ozaydin, 2006:**

Ozaydin M, Varol E, Aslan SM, Kucuktepe Z, Dogan A, Ozturk M, Altinbas A Effect of atorvastatin on the recurrence rates of atrial fibrillation after electrical cardioversion. *Am J Cardiol* 2006;97:1490-3 [[16679090](#)] [10.1016/j.amjcard.2005.11.082](#)

### **Ueng, 2003:**

Ueng KC, Tsai TP, Yu WC, Tsai CF, Lin MC, Chan KC, Chen CY, Wu DJ, Lin CS, Chen SA Use of enalapril to facilitate sinus rhythm maintenance after external cardioversion of long-standing persistent atrial fibrillation. Results of a prospective and controlled study. *Eur Heart J* 2003;24:2090-8 [[14643269](#)]

### **Madrid, 2002:**

Madrid AH, Bueno MG, Rebollo JM, Marn I, Pea G, Bernal E, Rodriguez A, Cano L, Cano JM, Cabeza P, Moro C Use of irbesartan to maintain sinus rhythm in patients with long-lasting persistent atrial fibrillation: a prospective and randomized study. *Circulation* 2002;106:331-6 [[12119249](#)]

### **Tveit, 2004:**

Tveit A, Grundtvig M, Gundersen T, Vanberg P, Semb AG, Holt E, Gullestad L Analysis of pravastatin to prevent recurrence of atrial fibrillation after electrical cardioversion. *Am J Cardiol* 2004;93:780-2 [[15019894](#)] [10.1016/j.amjcard.2003.12.009](#)

### **BAATAF (warfarin vs no treatment), 1990:**

The effect of low-dose warfarin on the risk of stroke in patients with nonrheumatic atrial fibrillation. The Boston Area Anticoagulation Trial for Atrial Fibrillation Investigators *N Engl J Med*. 1990 Nov 29;323(22):1505-11 [[2233931](#)]

### **SAFT(warfarin low dose + aspirin vs no treatment), 2003:**

Edvardsson N, Juul-Moller S, Omblus R, Pehrsson K Effects of low-dose warfarin and aspirin versus no treatment on stroke in a medium-risk patient population with atrial fibrillation. *J Intern Med* 2003 Jul;254:95-101 [[12823646](#)]

Edvardsson N, Juul-Moller S, Omblus R, Pehrsson K Effects of low-dose warfarin and aspirin versus no treatment on stroke in a medium-risk patient population with atrial fibrillation. *J Intern Med* 2003 Jul;254:95-101 [[12823646](#)]

### **AFASAK (warfarin standard dose vs control), 1989:**

Petersen P, Boysen G, Godtfredsen J, Andersen ED, Andersen B Placebo-controlled, randomised trial of warfarin and aspirin for prevention of thromboembolic complications in chronic atrial fibrillation. The Copenhagen AFASAK study. *Lancet* 1989 Jan 28;1:175-9 [[2563096](#)]

### **SPAF (warfarin standard dose), 1991:**

Stroke Prevention in Atrial Fibrillation Study. Final results *Circulation*. 1991 Aug;84(2):527-39. [[1860198](#)]

### **Van Gelder, 1989:**

Van Gelder IC, Crijns HJ, Van Gilst WH, Van Wijk LM, Hamer HP, Lie KI Efficacy and safety of flecainide acetate in the maintenance of sinus rhythm after electrical cardioversion of chronic atrial fibrillation or atrial flutter. *Am J Cardiol* 1989;64:1317-21 [[2511744](#)]

Abstracts from the 61st scientific sessions. American Heart Association. Washington, DC, November 14-17, 1988. *Circulation* 1988;78:IIA-IIIG, III-II775 [[3168202](#)]

### **Channer, 2004:**

Channer KS, Birchall A, Steeds RP, Walters SJ, Yeo WW, West JN, Muthusamy R, Rhoden WE, Saeed BT, Batin P, Brooksby WP, Wilson I, Grant S A randomized placebo-controlled trial of pre-treatment and short- or long-term maintenance therapy with amiodarone supporting DC cardioversion for persistent atrial fibrillation. *Eur Heart J* 2004;25:144-50 [[14720531](#)]

**GEFACA, 2001:**

Galpern J, Elizari MV, Chiale PA, Molina RT, Ledesma R, Scapn AO, Vzquez Blanco M Efficacy of amiodarone for the termination of chronic atrial fibrillation and maintenance of normal sinus rhythm: a prospective, multicenter, randomized, controlled, double blind trial. *J Cardiovasc Pharmacol Ther* 2001;6:341-50 [[11907636](#)]

**Kochiadakis (amiodarone vs placebo), 2000:**

Kochiadakis GE, Igoumenidis NE, Marketou ME, Kaleboubas MD, Simantirakis EN, Vardas PE Low dose amiodarone and sotalol in the treatment of recurrent, symptomatic atrial fibrillation: a comparative, placebo controlled study. *Heart* 2000;84:251-7 [[10956284](#)]

Kochiadakis GE, Igoumenidis NE, Marketou ME, Solomou MC, Kanoupakis EM, Vardas PE Low-dose amiodarone versus sotalol for suppression of recurrent symptomatic atrial fibrillation. *Am J Cardiol* 1998;81:995-8 [[9576159](#)]

Kochiadakis GE, Marketou ME, Igoumenidis NE, Chrysostomakis SI, Mavrakis HE, Kaleboubas MD, Vardas PE Amiodarone, sotalol, or propafenone in atrial fibrillation: which is preferred to maintain normal sinus rhythm? *Pacing Clin Electrophysiol* 2000;23:1883-7 [[11139949](#)]

**SAFE-T (amiodarone vs placebo), 2005:**

Singh BN, Singh SN, Reda DJ, Tang XC, Lopez B, Harris CL, Fletcher RD, Sharma SC, Atwood JE, Jacobson AK, Lewis HD Jr, Raisch DW, Ezekowitz MD Amiodarone versus sotalol for atrial fibrillation. *N Engl J Med* 2005;352:1861-72 [[15872201](#)]

Singh SN, Singh BN, Reda DJ, Fye CL, Ezekowitz MD, Fletcher RD, Sharma SC, Atwood JE, Jacobson AK, Lewis HD Jr, Antman EM, Falk RH, Lopez B, Tang XC Comparison of sotalol versus amiodarone in maintaining stability of sinus rhythm in patients with atrial fibrillation (Sotalol-Amiodarone Fibrillation Efficacy Trial [Safe-T]). *Am J Cardiol* 2003;92:468-72 [[12914883](#)]

**SMART, 2002:**

Atarashi H, Inoue H, Fukunami M, Sugi K, Hamada C, Origasa H Double-blind placebo-controlled trial of aprindine and digoxin for the prevention of symptomatic atrial fibrillation. *Circ J* 2002;66:553-6 [[12074271](#)]

**EAFIT, 1993:**

Secondary prevention in non-rheumatic atrial fibrillation after transient ischaemic attack or minor stroke. EAFIT (European Atrial Fibrillation Trial) Study Group. *Lancet*. 1993 Nov 20;342(8882):1255-62 [[7901582](#)]

**AFASAK (aspirin vs placebo), 1989:**

Petersen P, Boysen G, Godtfredsen J, Andersen ED, Andersen B Placebo-controlled, randomised trial of warfarin and aspirin for prevention of thromboembolic complications in chronic atrial fibrillation. The Copenhagen AFASAK study. *Lancet* 1989 Jan 28;1:175-9 [[2563096](#)]

**SPAF (aspirin , warfarin eligible arm), 1991:**

Stroke Prevention in Atrial Fibrillation Study. Final results *Circulation*. 1991 Aug;84(2):527-39. [[1860198](#)]

**SPAF (aspirin,warfarin ineligible arm), 1991:**

Stroke Prevention in Atrial Fibrillation Study. Final results *Circulation*. 1991 Aug;84(2):527-39. [[1860198](#)]

**ASAP, 2003:**

Connolly SJ, Schnell DJ, Page RL, Wilkinson WE, Marcello SR, Pritchett EL Dose-response relations of azimilide in the management of symptomatic, recurrent, atrial fibrillation. *Am J Cardiol* 2001;88:974-9 [[11703992](#)]

Connolly SJ, Schnell DJ, Page RL, Wilkinson WE, Marcello SR, Pritchett EL Symptoms at the time of arrhythmia recurrence in patients receiving azimilide for control of atrial fibrillation or flutter: results from randomized trials. *Am Heart J* 2003;146:489-93 [[12947368](#)]

Page RL, Tilsch TW, Connolly SJ, Schnell DJ, Marcello SR, Wilkinson WE, Pritchett EL Asymptomatic or "silent" atrial fibrillation: frequency in untreated patients and patients receiving azimilide. *Circulation* 2003;107:1141-5 [[12615792](#)]

Pritchett EL, Page RL, Connolly SJ, Marcello SR, Schnell DJ, Wilkinson WE Antiarrhythmic effects of azimilide in atrial fibrillation: efficacy and dose-response. Azimilide Supraventricular Arrhythmia Program 3 (SVA-3) Investigators. *J Am Coll Cardiol* 2000;36:794-802 [[10987602](#)]

Page RL, Connolly SJ, Wilkinson WE, Marcello SR, Schnell DJ, Pritchett EL Antiarrhythmic effects of azimilide in paroxysmal supraventricular tachycardia: efficacy and dose-response. *Am Heart J* 2002;143:643-9 [[11923801](#)]

**CAPRAF (Tveit), 2007:**

Tveit A, Grundvold I, Olufsen M, Seljeflot I, Abdelnoor M, Arnesen H, Smith P Candesartan in the prevention of relapsing atrial fibrillation. *Int J Cardiol* 2007;120:85-91 [[17113170](#)]

**CHARM (AF ancillary study), 2005:**

McMurray JJ, Ostergren J, Swedberg K, Granger CB, Held P, Michelson EL, Olofsson B, Yusuf S, Pfeffer MA Effects of candesartan in patients with chronic heart failure and reduced left-ventricular systolic function taking angiotensin-converting-enzyme inhibitors: the CHARM-Added trial. *Lancet* 2003;362:767-71 [[13678869](#)] [10.1016/S0140-6736\(03\)14283-3](#)

**Karlson, 1998:**

Karlson BW, Torstensson I, Abjrn C, Jansson SO, Peterson LE Disopyramide in the maintenance of sinus rhythm after electroconversion of atrial fibrillation. A placebo-controlled one-year follow-up study. *Eur Heart J* 1988;9:284-90 [[3289932](#)]

Karlson BW, Torstensson I, Abjrn C, Kallryd A, Jonsson J, Jansson SO, Peterson LE [Preventive disopyramide after electroconversion of atrial fibrillation—a good alternative] *Lakartidningen* 1991;88:2242-5 [[2056838](#)]

**Lloyd (Disopyramide vs placebo), 1984:**

**PALLAS, 2011:**

Connolly SJ, Camm AJ, Halperin JL, Joyner C, Alings M, Amerena J, Atar D, Avezum A, Blomstrm P, Borggreffe M, Budaj A, Chen SA, Ching CK, Commerford P, Dans A, Davy JM, Delacrtaz E, Di Pasquale G, Diaz R, Dorian P, Flaker G, Golitsyn S, Gonzalez-Hermosil Dronedarone in High-Risk Permanent Atrial Fibrillation. *N Engl J Med* 2011 Nov 14;: [[22082198](#)] [10.1056/NEJMoa1109867](#)

Connolly SJ, Camm AJ, Halperin JL, Joyner C, Alings M, Amerena J, Atar D, Avezum A, Blomstrm P, Borggreffe M, Budaj A, Chen SA, Ching CK, Commerford P, Dans A, Davy JM, Delacrtaz E, Di Pasquale G, Diaz R, Dorian P, Flaker G, Golitsyn S, Gonzalez-Hermosil Dronedarone in High-Risk Permanent Atrial Fibrillation. *N Engl J Med* 2011 Nov 14;: [[22082198](#)] [10.1056/NEJMoa1109867](#)

**ADONIS, 2007:**

Singh BN, Connolly SJ, Crijns HJ, Roy D, Kowey PR, Capucci A, Radzik D, Aliot EM, Hohnloser SH Dronedarone for maintenance of sinus rhythm in atrial fibrillation or flutter. *N Engl J Med* 2007 Sep 6;357:987-99 [[17804843](#)]

**ATHENA, 2009:**

Hohnloser SH, Crijns HJ, van Eickels M, et al. The ATHENA trial: Effects of dronedarone on cardiovascular hospitalization and death in patients with atrial fibrillation or flutter. HRS Annual Scientific Sessions; May 14-17, 2008, San Francisco

Hohnloser SH, Crijns HJ, van Eickels M, Gaudin C, Page RL, Torp-Pedersen C, Connolly SJ Effect of dronedarone on cardiovascular events in atrial fibrillation. *N Engl J Med* 2009 Feb 12;360:668-78 [[19213680](#)]

**DAFNE, 2003:**

Touboul P, Brugada J, Capucci A, Crijns HJ, Edvardsson N, Hohnloser SH Dronedarone for prevention of atrial fibrillation: a dose-ranging study. *Eur Heart J* 2003;24:1481-7 [[12919771](#)]

**ERATO, 2008:**

Davy JM, Herold M, Hognlund C, Timmermans A, Alings A, Radzik D, Van Kempen L Dronedarone for the control of ventricular rate in permanent atrial fibrillation: the Efficacy and safety of dRonedArone for the cOntrol of ventricular rate during atrial fibrillation (ERATO) study. *Am Heart J* 2008 Sep;156:527.e1-9 [[18760136](#)]

**EURIDIS, 2007:**

Singh BN, Connolly SJ, Crijns HJ, Roy D, Kowey PR, Capucci A, Radzik D, Aliot EM, Hohnloser SH Dronedarone for maintenance of sinus rhythm in atrial fibrillation or flutter. *N Engl J Med* 2007;357:987-99 [[17804843](#)]

**EURIDIS ADONIS (pooled analysis), 2009:**

Singh BN, Connolly SJ, Crijns HJ, Roy D, Kowey PR, Capucci A, Radzik D, Aliot EM, Hohnloser SH *N Engl J Med* 2007 Sep 6;357:987-99 [[17804843](#)]

**SOLVD (AF ancillary study), 2003:**

Vermes E, Tardif JC, Bourassa MG, Racine N, Levesque S, White M, Guerra PG, Ducharme A Enalapril decreases the incidence of atrial fibrillation in patients with left ventricular dysfunction: insight from the Studies Of Left Ventricular Dysfunction (SOLVD) trials. *Circulation* 2003;107:2926-31 [[12771010](#)] [10.1161/01.CIR.0000072793.81076.D4](#)

**Carunchio (flecainide vs placebo), 1995:**

Carunchio A, Fera MS, Mazza A, Burattini M, Greco G, Galati A, Ceci V [A comparison between flecainide and sotalol in the prevention of recurrences of paroxysmal atrial fibrillation] *G Ital Cardiol* 1995;25:51-68 [[7642012](#)]

**ACTIVE I, 2009:**

Yusuf S, Healey JS, Pogue J, Chrolavicius S, Flather M, Hart RG, Hohnloser SH, Joyner CD, Pfeffer MA, Connolly SJ Irbesartan in patients with atrial fibrillation. *N Engl J Med* 2011;364:928-38 [[21388310](#)] [10.1056/NEJMoa1008816](#)

Yusuf S, Healey JS, Pogue J, Chrolavicius S, Flather M, Hart RG, Hohnloser SH, Joyner CD, Pfeffer MA, Connolly SJ Irbesartan in patients with atrial fibrillation. *N Engl J Med* 2011 Mar 10;364:928-38 [[21388310](#)]

**P-OM3 (Kowey), 2010:**

Kowey PR, Reiffel JA, Ellenbogen KA, Naccarelli GV, Pratt CM Efficacy and Safety of Prescription Omega-3 Fatty Acids for the Prevention of Recurrent Symptomatic Atrial Fibrillation: A Randomized Controlled Trial. *JAMA* 2010 Nov 15;: [[21078810](#)] [10.1001/jama.2010.1735](#)

**EAFIT, 1993:**

Secondary prevention in non-rheumatic atrial fibrillation after transient ischaemic attack or minor stroke. EAFIT (European Atrial Fibrillation Trial) Study Group. *Lancet*. 1993 Nov 20;342(8882):1255-62 [[7901582](#)]

**Okishige, 2000:**

Okishige K, Nishizaki M, Azegami K, Igawa M, Yamawaki N, Aonuma K Pilsicainide for conversion and maintenance of sinus rhythm in chronic atrial fibrillation: a placebo-controlled, multicenter study. *Am Heart J* 2000;140:e13 [[10966544](#)]

**Bellandi (propafenone vs placebo), 2001:**

Bellandi F, Simonetti I, Leoncini M, Frascarelli F, Giovannini T, Maioli M, Dabizzi RP Long-term efficacy and safety of propafenone and sotalol for the maintenance of sinus rhythm after conversion of recurrent symptomatic atrial fibrillation. *Am J Cardiol* 2001;88:640-5 [[11564387](#)]

Bellandi F, Dabizzi RP, Niccoli L, Cantini F, Palchetti R [Propafenone and sotalol: long-term efficacy and tolerability in the prevention of paroxysmal atrial fibrillation. A placebo-controlled double-blind study] *G Ital Cardiol* 1996;26:379-90 [[8707022](#)]

Bellandi F, Dabizzi RP, Niccoli L, Cantini F, Palchetti R [Propafenone and sotalol: long-term efficacy and tolerability in the prevention of paroxysmal atrial fibrillation. A placebo-controlled double-blind study] *G Ital Cardiol* 1996;26:379-90 [[8707022](#)]

**Dogan, 2004:**

Dogan A, Ergene O, Nazli C, Kinay O, Altinbas A, Ucarci Y, Ergene U, Ozaydin M, Gedikli O Efficacy of propafenone for maintaining sinus rhythm in patients with recent onset or persistent atrial fibrillation after conversion: a randomized, placebo-controlled study. *Acta Cardiol* 2004;59:255-61 [[15255456](#)]

**Kochiadakis b (propafenone vs placebo), 2004:**

Kochiadakis GE, Igoumenidis NE, Hamilos ME, Tzerakis PG, Klapsinos NC, Chlouverakis GI, Vardas PE Sotalol versus propafenone for long-term maintenance of normal sinus rhythm in patients with recurrent symptomatic atrial fibrillation. *Am J Cardiol* 2004;94:1563-6 [[15589019](#)]

Kochiadakis GE, Igoumenidis NE, Hamilos ME, Tzerakis PG, Klapsinos NC, Chlouverakis GI, Vardas PE *Am J Cardiol* 2004;94:1563-6 [[15589019](#)] [10.1016/j.amjcard.2004.08.041](#)

**RAFT, 2003:**

Pritchett EL, Page RL, Carlson M, Undesser K, Fava G Efficacy and safety of sustained-release propafenone (propafenone SR) for patients with atrial fibrillation. *Am J Cardiol* 2003;92:941-6 [[14556870](#)]

**Stroobandt, 1997:**

Stroobandt R, Stiels B, Hoebrechts R Propafenone for conversion and prophylaxis of atrial fibrillation. Propafenone Atrial Fibrillation Trial Investigators. *Am J Cardiol* 1997;79:418-23 [[9052343](#)]

**GISSI HF (subgroup and ancillary study), 2009:**

Maggioni AP, Fabbri G, Lucci D, Marchioli R, Franzosi MG, Latini R, Nicolosi GL, Porcu M, Cosmi F, Stefanelli S, Tognoni G, Tavazzi L Effects of rosuvastatin on atrial fibrillation occurrence: ancillary results of the GISSI-HF trial. *Eur Heart J* 2009 Oct;30:2327-36 [[19717850](#)]

**Bellandi (sotalol vs placebo), 2001:**

**Benditt, 1999:**

Benditt DG, Williams JH, Jin J, Deering TF, Zucker R, Browne K, Chang-Sing P, Singh BN Maintenance of sinus rhythm with oral d,l-sotalol therapy in patients with symptomatic atrial fibrillation and/or atrial flutter. d,l-Sotalol Atrial Fibrillation/Flutter Study Group. *Am J Cardiol* 1999;84:270-7 [[10496434](#)]

**Carunchio (sotalol vs placebo), 1995:**

**Kochiadakis (sotalol vs placebo), 2000:**

**Kochiadakis b (sotalol vs placebo), 2004:**

Kochiadakis GE, Igoumenidis NE, Hamilos ME, Tzerakis PG, Klapsinos NC, Chlouverakis GI, Vardas PE *Am J Cardiol* 2004;94:1563-6 [[15589019](#)] [10.1016/j.amjcard.2004.08.041](#)

**PAFAC (sotalol vs placebo), 2004:**

Fetsch T, Bauer P, Engberding R, Koch HP, Lukl J, Meinertz T, Oeff M, Seipel L, Trappe HJ, Treese N, Breithardt G Prevention of atrial fibrillation after cardioversion: results of the PAFAC trial. *Eur Heart J* 2004;25:1385-94 [[15302102](#)]



**SAFE-T (sotalol vs placebo), 2005:**

Singh BN, Singh SN, Reda DJ, Tang XC, Lopez B, Harris CL, Fletcher RD, Sharma SC, Atwood JE, Jacobson AK, Lewis HD Jr, Raisch DW, Ezekowitz MD Amiodarone versus sotalol for atrial fibrillation. *N Engl J Med* 2005;352:1861-72 [[15872201](#)] [10.1056/NEJMoa041705](#)

Singh BN, Singh SN, Reda DJ, Tang XC, Lopez B, Harris CL, Fletcher RD, Sharma SC, Atwood JE, Jacobson AK, Lewis HD Jr, Raisch DW, Ezekowitz MD Amiodarone versus sotalol for atrial fibrillation. *N Engl J Med* 2005;352:1861-72 [[15872201](#)] [10.1056/NEJMoa041705](#)

**Singh, 1991:**

Singh S, Saini RK, DiMarco J, Kluger J, Gold R, Chen YW Efficacy and safety of sotalol in digitalized patients with chronic atrial fibrillation. The Sotalol Study Group. *Am J Cardiol* 1991;68:1227-30 [[1951086](#)]

**SOPAT (sotalol vs placebo), 2004:****TRACE (AF ancillary study), 1999:**

Pedersen OD, Bagger H, Kober L, Torp-Pedersen C Trandolapril reduces the incidence of atrial fibrillation after acute myocardial infarction in patients with left ventricular dysfunction. *Circulation* 1999;100:376-80 [[10421597](#)]

**Val-HeFT (AF ancillary study), 2003:**

Maggioni ALR, Carson PE, et al Valsartan reduces the incidence of atrial fibrillation in the patients with heart failure in the Val-HeFT Trial *Circulation* 2003;108:507

**GISSI-AF (Disertori), 2009:**

Disertori M, Latini R, Barlera S, Franzosi MG, Staszewsky L, Maggioni AP, Lucci D, Di Pasquale G, Tognoni G Valsartan for prevention of recurrent atrial fibrillation. *N Engl J Med* 2009 Apr 16;360:1606-17 [[19369667](#)]

**SPINAF (warfarin vs placebo), 1992:**

Ezekowitz MD, Bridgers SL, James KE, Carliner NH, Colling CL, Gornick CC, Krause-Steinrauf H, Kurtzke JF, Nazarian SM, Radford MJ Warfarin in the prevention of stroke associated with nonrheumatic atrial fibrillation. Veterans Affairs Stroke Prevention in Nonrheumatic Atrial Fibrillation Investigators. *N Engl J Med* 1992 Nov 12;327:1406-12 [[1406859](#)]

**CAFA, 1991:**

Connolly SJ, Laupacis A, Gent M, Roberts RS, Cairns JA, Joyner C Canadian Atrial Fibrillation Anticoagulation (CAFA) Study. *J Am Coll Cardiol* 1991 Aug;18:349-55 [[1856403](#)]

## 10 acute coronary syndrome

Trial	Treatments	Patients	Trials design and methods
<b>triflusal vs aspirin</b>			
<a href="#">TIM , 2000</a> n=1135/1140 follow-up: 35 days	triflusal 600 mg daily versus aspirine 300 mg daily	AMI within less than 24 h of symptom onsete	Parallel groups double blind Portugal, Spain, Italy
<b>aspirin vs control</b>			
<a href="#">Huddinge , 1988</a> n=10/10 follow-up: 30d (12m)	aspirin 500mg/d starting 12 h after admissionand and then intermittently every third day for one month versus no aspirin	patients with acute myocardial infarction	Parallel groups open
<a href="#">ATACS-pilot , 1990</a> n=37/24 follow-up: 3m	Aspirin 80mg/d (Heparin + Warfarin) versus full-dose heparin followed by warfarin	acute coronary syndromes	

continued...



<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
Frankfurt , 1976 n=25/28 follow-up: 14d	-	-	Parallel groups
<b>dazoxiben vs control</b>			
Jones , 1987 n=60/60 follow-up: 1m	-	-	Parallel groups
<b>hyperbaric oxygen vs control</b>			
Sharifi , 2004 n=NA follow-up:	-	after percutaneous coronary intervention for acute myocardial infarction or unstable angina pectoris	
Swift , 1992 n=NA follow-up:	-	patients within 1 week of acute myocardial infarction	
Thurston , 1973 n=NA follow-up:	-	acute myocardial infarction	
Hot MI , 1997 n=112 follow-up:	-	Patients with an acute myocardial infarction who received recombinant tissue plasminogen activator	
HOT MI pilot , 1997 n=66 follow-up:	-	Patients with an acute myocardial infarction (AMI) who received recombinant tissue plasminogen activator	
<b>oxygen therapy vs control</b>			
Rawles , 1976 n=NA follow-up:	oxygen administered by MC mask throughout the first 24 hours versus air	myocardial infarction	
Ukholkina , 2005 n=NA follow-up:	-	patients with acute myocardial infarction	
Wilson , 1997 n=NA follow-up:	oxygen therapy versus control	patients presenting within 24 hours of onset of myocardial infarction	
<b>sulfinpyrazone vs control</b>			
Dutch sulphinpyrazone , 1986 n=50/50 follow-up: 21d	-	-	Parallel groups
<b>supersaturated oxygen vs control</b>			

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>AMIHOT II , 2000</b> [NCT00175058] n=222/79 follow-up:	90-minute intracoronary supersaturated oxygen (SSO(2)) infusion in the left anterior descending artery infarct territory versus control	patients with anterior ST-segment elevation myocardial infarction undergoing percutaneous coronary intervention within 6 hours of symptom onset	
<b>AMIHOT , 2007</b> n=NA follow-up:	hyperoxemic reperfusion for 90 min using intracoronary aqueous oxygen versus normoxemic blood autoreperfusion	patients with acute anterior or large inferior AMI undergoing primary or rescue PCI (<24 h from symptom onset) and successful PCI	
<b>coumadin vs control (on top of aspirin)</b>			
<b>ASPECT-2 (coumadin+asp vs asp) , 2002</b> n=333/336 follow-up: 1 year	coumadin(INR mean 2.4) +aspirin versus aspirin	UA, AMI	open the Netherlands
<b>UFH, warfarin vs control (on top of aspirin)</b>			
<b>ATACS (Cohen) , 1994</b> n=105/109 follow-up: 12 weeks	aspirin 162.5 mg daily plus heparin (activated partial thromboplastin time, two times control) followed by aspirin 162.5 mg daily plus warfarin (international normalized ratio, 2 to 3) for 12 weeks. versus aspirin alone (162.5 mg daily) for 12 weeks.	patients with unstable rest angina or non-Q-wave myocardial infarction with last episode of pain within 48 hours of randomization and who were nonprior aspirin users	Parallel groups single blind
<b>Cohen (ATACS pilot) (heparin+aspirin vs asp) , 1990</b> n=37/32 follow-up: 12 weeks	aspirin (80 mg/day) plus heparin and then warfarin versus aspirin (325 mg/day)	Patients between 21 and 75 years with unstable angina or non-Q-wave MI with last episode of pain within 48 hours of screening.	Parallel groups open
<b>warfarin vs control (on top of aspirin)</b>			
<b>ATACS (pilot study) (warfarin vs control) , 1990</b> n=37/32 follow-up: 65279;3 months	heparin/warfarin target INR 65279;3-4.5 + aspirin versus aspirin alone	65279;UA, NSTEMI	open
<b>ATACS , 1994</b> n=105/109 follow-up: 3 months	heparin/warfarin (INR median 2.3) + aspirin versus aspirin	UA, NSTEMI	open
<b>CARS , 1997</b> n=5410/3393 follow-up: 14 months	warfarin (INR mean 1.5) (3 mg warfarin or 1 mg warfarin with 80 mg aspirin) versus aspirin 160 mg/d	AMI	

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>OASIS Pilot (phase 1) , 1998</b> n=155/154 follow-up: 6 months	warfarin 3mg/d for 6 months (INR mean 1.5) versus control	UA, NSTEMI	open
<b>OASIS Pilot (phase 2) , 1998</b> n=98/99 follow-up: 3 months	warfarin adjusted dose (INR mean 2.3) for 3 months versus standard treatment	UA, NSTEMI	open
<b>OASIS-2 Warfarin Substudy , 2001</b> n=1848/1864 follow-up: 5 months	warfarin target INR 65279;22.5 for 5 months +aspirin versus control	UA	open
<b>APRICOT-2 , 2002</b> n=135/139 follow-up: 3 months	moderate-intensity coumarin target INR 2-3 (+aspirin) versus aspirin	STEMI	
<b>CHAMP , 2002</b> n=2522/2537 follow-up: 2.7 years	-	AMI	
<b>WARIS , 2002</b> n=1208/1206 follow-up: 4 years	-	AMI	
<b>LoWASA , 2004</b> n=1659/1641 follow-up: 5 years	-	AMI	
<b>Zibaenezhad , 2004</b> n=70/70 follow-up: 1 year	-	AMI	
<b>bivalirudin vs heparin + GP2b3a inhibitors</b>			
<b>ACUTY (biva alone vs hep+aGP2b3a) , 2006</b> [NCT00093158] n=4612/4603 follow-up: 30 days	bivalirudin alone versus unfractionated heparin or enoxaparin plus a glycoprotein IIb/IIIa inhibitor	in patients with moderate- or high-risk acute coronary syndromes who were undergoing an early invasive strategy.	Parallel groups double blind 17 countries worldwide
<b>ACUTY (sub groups PCI, bivalirudin alone) import , 2007</b> n=2619/2561 follow-up: 30 days	bivalirudin alone versus heparin (either unfractionated or enoxaparin) plus glycoprotein IIb/IIIa inhibitors	patients with moderate and high-risk acute coronary syndromes undergoing percutaneous coronary intervention after angiography (sub group).	Factorial plan open
<b>bivalirudin + GP2b3a inhibitors vs heparin + GP2b3a inhibitors</b>			

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>ACUTY (biva+aGP2b3a vs hep+aGP2b3a) , 2006</b> [NCT00093158] n=4604/4603 follow-up: 30 days	bivalirudin plus a glycoprotein IIb/IIIa inhibitor versus unfractionated heparin or enoxaparin plus a glycoprotein IIb/IIIa inhibitor	in patients with moderate- or high-risk acute coronary syndromes who were undergoing an early invasive strategy.	double blind 17 countries worldwide
<b>ACUTY (sub groups PCI, bivalirudin +aGP2b3a) import , 2007</b> n=2609/2561 follow-up: 30 days	bivalirudin + versus heparin (either unfractionated or enoxaparin) plus glycoprotein IIb/IIIa inhibitors	patients with moderate and high-risk acute coronary syndromes undergoing percutaneous coronary intervention after angiography.	open
<b>anistreplase vs placebo</b>			
<b>UNASEM , 1992</b> n=80/79 follow-up: hospital stay, 1y	anistreplase IV 30 UI over 5 minutes versus placebo	Patients without a previous myocardial infarction, with a typical history of unstable angina and ECG abnormalities indicative of ischemia	Parallel groups double blind Europe
<b>apixaban vs placebo</b>			
<b>APPRAISE 2 , 2011</b> [NCT00831441] n=3705/3687 follow-up: 8 months	apixaban 5mg twice daily versus placebo	patients with a recent acute coronary syndrome and at least two additional risk factors for recurrent ischemic events	Parallel groups double blind 39 countries
<b>APPRAISE-1 (10mg od) , 2009</b> [NCT00313300] n=318/611 follow-up: 6 months	apixaban 10 mg once daily versus placebo	patients with a recent ST-elevation or nonST-elevation acute coronary syndrome(<7 days)	Parallel groups double blind Europe, Middle East, North America
<b>APPRAISE-1 (2.5 mg bid) , 2009</b> [NCT00313300 ] n=NA follow-up: 6 months	Apixaban 2.5mg twice daily versus placebo	patients with a recent ST-elevation or nonST-elevation acute coronary syndrome(<7 days)	double blind Europe, Middle East, North America
<b>APPRAISE japan ongoing</b> [NCT00852397] n=NA follow-up:	2 doses of apixaban (2.5 mg BID and 5.0 mg BID) for 24 weeks in combination with standard therapy (aspirin and /or additional antiplatelet therapy) versus placebo	patients with recent (<=7 days) acute coronary syndrome	double-blind Japan
<b>aspirin vs placebo</b>			
<b>VA-main , 1983</b> n=661/677 follow-up: 3m	Aspirin 324mg/d versus placebo	men with unstable angina	double blind

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>ISIS-pilot , 1987</b> n=313/306 follow-up: 1m	aspirin (325 mg on alternate days for 28 days) versus placebo	suspected acute myocardial infarction	Parallel groups double blind
<b>ISIS-2 , 1988</b> n=8587/8600 follow-up: 35d	160 mg/day enteric-coated aspirin for one month versus placebo	suspected acute myocardial up to 24h	Parallel groups double blind
<b>VA-pilot</b> <i>unpublished</i> n=26/24 follow-up: 3m	-	-	
<b>RISC , 1990</b> n=474/471 follow-up: 12m	Aspirin 75mg/d versus placebo	men with unstable coronary artery disease (unstable angina or non-Q wave myocardial infarction)	Factorial plan double blind Sweden
<b>Canadian (Aspirin vs PBO) , 1985</b> n=NA follow-up: 18m	Aspirin 1300mg/d versus placebo	patients with unstable angina	double blind
<b>ALDUSA-pilot</b> <i>unpublished</i> n=56/28 follow-up: 12m	-	-	
<b>Dutch-aspirin , 1990</b> n=50/50 follow-up: 3m	aspirin (100 mg/day) for 3 months versus placebo	patients with first anterior wall AMI	Parallel groups double blind
<b>Throux , 1988</b> n=121/118 follow-up: 6d (3m)	Aspirin 325 mg twice daily versus placebo	acute unstable angina	double blind
<b>APRICOT , 1993</b> n=107/95 follow-up: 3m	325 mg aspirin daily with discontinuation of heparin versus placebo	Patients treated with intravenous thrombolytic therapy followed by intravenous heparin and with patent infarct-related artery demonstrated at angiography within 48 hours	Parallel groups double blind The Netherlands
<b>aspirin + dipyridamol vs placebo</b>			
<b>Prandoni , 1991</b> n=44/44 follow-up: 12m	Aspirin 50mg/d + Dipyridamol 400mg/d versus placebo	patients with acute unstable angina	double blind
<b>aspirin + sulfapyrazone vs placebo</b>			
<b>Canadian (Aspirin + sulfapyrazone) , 1985</b> n=416/139 follow-up: 18m	Aspirin 1300mg/d + sulfapyrazone 800mg/d versus placebo	patients with unstable angina	double blind
<b>atopaxar vs placebo</b>			

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>LANCELOT ACS</b> n=603 follow-up:	400-mg loading dose of atopaxar followed by a daily dose of 50 mg, 100 mg, or 200 mg for 12 weeks versus placebo	unstable-angina or non-STEMI patients	Parallel groups
<b>J-LANCELOT , 2010</b> n=NA follow-up:	atopaxar at a loading dose of 400 mg followed by 50 mg per day, 100 mg per day, or 200 mg per day for 12 weeks versus atopaxar at a loading dose of 400 mg followed by placebo	patients with acute coronary syndrome (unstable angina and NSTEMI)	Parallel groups Japan
<b>atorvastatin vs placebo</b>			
<b>MIRACL , 2001</b> n=1538/1548 follow-up: 1 and 4 months	Atorvastatin, 80 mg (early initiation) versus Placebo	unstable angina or nonQ-wave acute MI	Parallel groups Double blind Europe, North America, South Africa, and Australasia
<b>dabigatran vs placebo</b>			
<b>REDEEM , 2009</b> <i>unpublished</i> [NCT00621855] n=1501/373 follow-up: 6 months	dabigatran 4 dosages (50mg twice daily, 75mg twice daily, 110mg twice daily, 150mg twice daily) versus placebo	patients with recent acute coronary syndromes (ST- or non-ST-elevation myocardial infarction)	Parallel groups double blind
<b>diltiazem vs placebo</b>			
<b>Gbel (Dutch study) , 1995</b> n=129 follow-up: ND	diltiazem intravenously versus glyceryl trinitrate intravenously	patients with unstable angina	Parallel groups double blind
<b>DRS , 1986</b> n=287/289 follow-up: ND	diltiazem 90 mg every six hours up to 14 days versus placebo	patients with non-Q-wave myocardial infarct, 24 to 72 hours after the onset of infarction	double blind
<b>fluvastatin vs placebo</b>			
<b>LIPS (sub groups) , 2002</b> n=417/407 follow-up: 1, 4, and 6 months	Fluvastatin, 80 mg versus Placebo	patients with unstable angina and successful first percutaneous coronary intervention	Parallel groups double blind Europe, Canada, and Brazil
<b>FLORIDA , 2002</b> n=265/275 follow-up: 1, 4, and 6 months	Fluvastatin, 80 mg (early initiation) versus Placebo	patients with an AMI and total cholesterol of <6.5 mmol.l	Parallel groups double blind The Netherlands

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>Czech trial</b> <i>ongoing</i> [NCT00171275] n=NA follow-up: 52 weeks	fluvastatin versus placebo	-	Parallel groups double blind
<b>intracoronary urokinase vs placebo</b>			
<b>TAUSA , 1994</b> n=232/237 follow-up: hospital stay	intracoronary urokinase 250000 UI or 500000 UI versus placebo	ischemic rest pain with or without a recent (<1 month) infarction	Parallel groups double blind USA
<b>pravastatin vs placebo</b>			
<b>LAMIL , 1997</b> n=36/33 follow-up: 1 and 3 months	Pravastatin, 10-20 mg (starting at D3) versus Placebo	patients suffering an acute myocardial infarction	Parallel groups double blind Belgium
<b>RECIFE , 1999</b> n=30/30 follow-up: 1.5 months	Pravastatin, 40 mg versus Placebo	Patients with acute myocardial infarction or unstable angina and total cholesterol levels at admission $\geq 5.2$ mmol/L or LDL $\geq 3.4$ mmol/L	Parallel groups double blind Canada
<b>PAIS , 2001</b> n=50/49 follow-up: 1 and 3 months	Pravastatin, 40 mg (initiated within 48 hours of hospital admission) versus Placebo	patients with acute coronary syndromes	Parallel groups double blind The Netherlands
<b>FACT , 2004</b> n=1710/1698 follow-up: 1 months	Pravastatin, 20-40 mg within 24 hours of the onset of symptoms in versus Placebo	patients with unstable angina, non-ST-segment elevation myocardial infarction, or ST-segment elevation myocardial infarction within 24 hours of the onset of symptoms	Parallel groups double blind Australia
<b>ranolazine vs placebo</b>			
<b>MERLIN TIMI 36 , 2007</b> [NCT00099788] n=3279/3281 follow-up: median 11.4 months	ranolazine 1000 mg twice daily for the duration of the trial (initially 200 mg intravenously for 1 hour, followed by an 80 mg/h intravenous infusion) versus placebo	Hospitalized with NSTEMI-ACS; ischemic symptoms at rest within 48 hours; and at least one indicator of moderate to high risk, defined as elevated troponin or creatinine kinase-myocardial band, ST-depression $>0.1$ mV, diabetes, or TIMI risk score for unstable angina/NSTEMI $\geq 3$	Parallel groups Double blind 17 countries
<b>rivaroxaban 2.5mg vs placebo</b>			
<b>ATLAS ACS-TIMI 46 (2.5mg) , 2009</b> [NCT00402597] n=152/1160 follow-up: 6 months	rivaroxaban 2.5 mg twice daily versus placebo	recent ACS patients treated with aspirin alone (n=761) or aspirin plus clopidogrel (n=2730)	double blind 27 countries

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>ATLAS ACS 2 - TIMI 51 (2.5mg) , 2011</b> [NCT00809965] n=5174/5176 follow-up: 13 months	rivaroxaban 2.5 mg twice daily in addition to standard care versus placebo	patients with a recent ACS	Parallel groups double blind 44 countries
<b>rivaroxaban 5mg vs placebo</b>			
<b>ATLAS ACS-TIMI 46 (5mg) , 2009</b> [NCT00402597] n=519/1160 follow-up: 6 months	rivaroxaban 5 mg twice daily versus placebo	recent ACS patients treated with aspirin alone (n=761) or aspirin plus clopidogrel (n=2730)	Parallel groups double blind 27 countries
<b>ATLAS ACS 2 - TIMI 51 (5mg) , 2011</b> [NCT00809965] n=5176/5176 follow-up: 13 months	rivaroxaban 5 mg twice daily in addition to standard care versus placebo	patients with a recent ACS	double blind 44 countries
<b>simvastatin vs placebo</b>			
<b>A to Z , 2004</b> n=2265/2232 follow-up: 4 months	Simvastatin, 40-80 mg early initiation versus Placebo	patient with an acute coronary syndrome (ACS)	Parallel groups Double aveugle 41 countries
<b>sulfinpyrazone vs placebo</b>			
<b>Canadian (sulfinpyrazone alone) , 1985</b> n=NA follow-up: 18m	sulfinpyrazone 800mg/d versus placebo	patients with unstable angina	double blind
<b>Wilcox , 1980</b> n=49/49 follow-up: 10d	Sulphinpyrazone 200 mg four times daily versus placebo	patients with acute myocardial infarction	Parallel groups
<b>Louvain sulphinpyrazone , 1983</b> n=15/14 follow-up: 7d	sulphinpyrazone, 4 x 200 mg daily for 7 days versus placebo	recent myocardial infarction	Parallel groups double blind
<b>t-PA vs placebo</b>			
<b>Nicklas , 1989</b> n=20/20 follow-up:	rt-PA, 150 mg/8 h versus placebo	patients with rest angina, angiographically documented coronary artery disease and pacing-induced ischemia	Parallel groups Double blind USA
<b>Gold , 1987</b> n=12/12 follow-up:	intravenous recombinant human tissue-type plasminogen activator (rt-PA). versus placebo	chest pain at rest with transient ST segment deviation of at least 1 mm	Parallel groups

continued...



<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>Williams , 1990</b> n=45/22 follow-up:	tissue-type plasminogen activator (rt-PA) (0.75 mg/kg over 1 hour or (0.75 mg/kg over 1 hour; total dose, 100 mg over 6 hours) versus placebo	rest angina and angiographic evidence of coronary stenosis	Parallel groups double blind USA
<b>Freeman , 1992</b> n=35/35 follow-up: in hospital	tissue-type plasminogen activator (t-PA) (0.49 MU/kg for 1 hour followed by 0.07 MU/kg per hour for 9 hours) versus placebo	patients with unstable angina	Parallel groups double blind USA
<b>van der Brand , 1991</b> n=19/17 follow-up: hospital stay	alteplase 100 mg in 3 h versus placebo	patients with angina at rest, despite bedrest and medical treatment	Parallel groups double blind The Netherlands
<b>charbonnier , 1992</b> n=25/25 follow-up:	rt-PA 100 mg/90 minutes (10 mg bolus + 90 mg/90 minutes) versus placebo	unstable angina pectoris	Parallel groups double blind
<b>Ardissino , 1990</b> n=12/12 follow-up: in hospital	recombinant tissue-type plasminogen activator (rt-PA) followed by heparin versus heparin alone	unstable angina refractory to conventional medical treatment	Parallel groups double blind Italy
<b>TIMI 3B , 1995</b> n=729/744 follow-up: 1 year	tissue-type plasminogen activator (t-PA) versus placebo	patients with unstable angina and non-Q wave myocardial infarction	Factorial plan Double blind
<b>Topol , 1988</b> n=20/20 follow-up: hospital stay	intravenous tissue plasminogen activator (t-PA) versus placebo	patients with angina at rest and provokable ischemia (pacing induced)	Parallel groups open USA
<b>TIMI 3A , 1993</b> n=150/156 follow-up: hospital stay	90-minute front-loaded infusion of t-PA (0.8 mg/kg i.v.; maximum, 80 mg) versus placebo	patients with unstable angina or non-Q wave myocardial infarction	Parallel groups double blind USA, canada

More details and results :

- cholesterol lowering intervention for acute coronary syndrome in early initiation at <http://www.trialresultscenter.org/go-Q21>
- myocardial revascularization for acute coronary syndrome in all type of patients at <http://www.trialresultscenter.org/go-Q22>
- antithrombotics for acute coronary syndrome in all type of patients at <http://www.trialresultscenter.org/go-Q24>
- antithrombotics for acute coronary syndrome in unstable angina at <http://www.trialresultscenter.org/go-Q35>
- myocardial revascularization for acute coronary syndrome in Elderly patients at <http://www.trialresultscenter.org/go-Q165>
- anticoagulant for acute coronary syndrome in All ACS (including AMI) at <http://www.trialresultscenter.org/go-Q167>

- anticoagulant for acute coronary syndrome in ACS (excluding AMI) at <http://www.trialresultscenter.org/go-Q168>
- antiplatelets drug for acute coronary syndrome in ACS (excluding AMI) at <http://www.trialresultscenter.org/go-Q169>
- antiplatelets drug for acute coronary syndrome in patients with scheduled percutaneous coronary intervention at <http://www.trialresultscenter.org/go-Q170>
- heparin (UFH or LMWH) for acute coronary syndrome in all type of patients at <http://www.trialresultscenter.org/go-Q171>
- calcium channel blockers for acute coronary syndrome in all type of patients at <http://www.trialresultscenter.org/go-Q222>
- fibrinolysis for acute coronary syndrome in all type of patients at <http://www.trialresultscenter.org/go-Q223>
- anti-anginal drugs for acute coronary syndrome in all type of patients at <http://www.trialresultscenter.org/go-Q264>
- direct factor Xa inhibitors for acute coronary syndrome in all type of patients at <http://www.trialresultscenter.org/go-Q345>
- antiplatelets drug for acute coronary syndrome in all type of patients at <http://www.trialresultscenter.org/go-Q346>
- antithrombotics for acute coronary syndrome in patients managed with an early invasive strategy at <http://www.trialresultscenter.org/go-Q347>
- antithrombotics for acute coronary syndrome in PCI sub group at <http://www.trialresultscenter.org/go-Q348>
- antithrombotics for acute coronary syndrome in patients with a recent ACS at <http://www.trialresultscenter.org/go-Q387>
- oxygen therapy for acute coronary syndrome in all type of patients at <http://www.trialresultscenter.org/go-Q428>
- New P2Y12 Inhibitors for acute coronary syndrome in all type of patients at <http://www.trialresultscenter.org/go-Q455>

## References

### **TIM, 2000:**

Cruz-Fernandez JM, Lopez-Bescos L, Garcia-Dorado D, Lopez Garcia-Aranda V, Cabads A, Martin-Jadraque L, Velasco JA, Castro-Beiras A, Torres F, Marfil F, Navarro E Randomized comparative trial of triflusal and aspirin following acute myocardial infarction. *Eur Heart J* 2000;21:457-65 [10681486]

### **Huddinge, 1988:**

Rasmanis G, Vesterqvist O, Gren K, Edhag O, Henriksson P Effects of intermittent treatment with aspirin on thromboxane and prostacyclin formation in patients with acute myocardial infarction. *Lancet* 1988;2:245-7 [2899236]

### **ATACS-pilot, 1990:**

Cohen M, Adams PC, Hawkins L, Bach M, Fuster V Usefulness of antithrombotic therapy in resting angina pectoris or non-Q-wave myocardial infarction in preventing death and myocardial infarction (a pilot study from the Antithrombotic Therapy in Acute Coronary Syndromes Study Group). *Am J Cardiol* 1990 Dec 1;66:1287-92 [2244556]

### **Frankfurt, 1976:**

Asasantin DVT nach Myokardinfarktp, imag Boehringer Ingelheim, 1976. (Boehringer Ingelheim internal report.)

### **Jones, 1987:**

Jones EW. A study of dazoxiben in the prevention of venous thrombosis after suspected myocardial infarction (MD Thesis).; Nottingham: Nottingham University, 1987:111-24

### **Sharifi, 2004:**

Sharifi M, Fares W, Abdel-Karim I, Koch JM, Sopko J, Adler D Usefulness of hyperbaric oxygen therapy to inhibit restenosis after percutaneous coronary intervention for acute myocardial infarction or unstable angina pectoris. *Am J Cardiol* 2004;93:1533-5 [15194029] 10.1016/j.amjcard.2004.03.009

Sharifi M, Fares W, Abdel-Karim I, Petrea D, Koch JM, Adler D, Sopko J Inhibition of restenosis by hyperbaric oxygen: a novel indication for an old modality. *Cardiovasc Radiat Med* 2002;3:124-6 [12974361]

### **Swift, 1992:**

Swift PC, Turner JH, Oxer HF, O'Shea JP, Lane GK, Woollard KV Myocardial hibernation identified by hyperbaric oxygen treatment and echocardiography in postinfarction patients: comparison with exercise thallium scintigraphy. *Am Heart J* 1992;124:1151-8 [1442480]

### **Thurston, 1973:**

Thurston JG, Greenwood TW, Bending MR, Connor H, Curwen MP A controlled investigation into the effects of hyperbaric oxygen on mortality following acute myocardial infarction. *Q J Med* 1973;42:751-70 [[4606106](#)]

**Hot MI, 1997:**

Shandling AH, Ellestad MH, Hart GB, Crump R, Marlow D, Van Natta B, Messenger JC, Strauss M, Stavitsky Y Hyperbaric oxygen and thrombolysis in myocardial infarction: the "HOT MI" pilot study. *Am Heart J* 1997;134:544-50 [[9327714](#)]

Stavitsky Y, Shandling AH, Ellestad MH, Hart GB, Van Natta B, Messenger JC, Strauss M, Dekleva MN, Alexander JM, Mattice M, Clarke D Hyperbaric oxygen and thrombolysis in myocardial infarction: the 'HOT MI' randomized multicenter study. *Cardiology* 1998;90:131-6 [[9778551](#)]

Laden G. HOT MI pilot study. Hyperbaric oxygen and thrombolysis in myocardial infarction *American Heart Journal* 1998;136(4 Pt 1):749.

**HOT MI pilot, 1997:**

Shandling AH, Ellestad MH, Hart GB, Crump R, Marlow D, Van Natta B, Messenger JC, Strauss M, Stavitsky Y Hyperbaric oxygen and thrombolysis in myocardial infarction: the "HOT MI" pilot study. *Am Heart J* 1997;134:544-50 [[9327714](#)]

**Rawles, 1976:**

Rawles JM, Kenmure AC Controlled trial of oxygen in uncomplicated myocardial infarction. *Br Med J* 1976;1:1121-3 [[773507](#)]

**Ukholkina, 2005:**

Ukholkina GB, Kostianov Iiu, Kuchkina NV, Grendo EP, Gofman IaB [Effect of oxygenotherapy used in combination with reperfusion in patients with acute myocardial infarction] *Kardiologija* 2005;45:59 [[16007057](#)]

**Wilson, 1997:**

Wilson AT, Channer KS Hypoxaemia and supplemental oxygen therapy in the first 24 hours after myocardial infarction: the role of pulse oximetry. *J R Coll Physicians Lond* 1997;31:657-61 [[9409501](#)]

**Dutch sulphinpyrazone, 1986:**

Funke Kpper AJ, Verheugt FWA, Jaarsma W, Roos JP.age/pj Funke Kpper AJ, Verheugt FWA, Jaarsma W, Roos JP. Failure of sulphinpyrazone to prevent left ventricular thrombosis in patients with AMI treated with oral anticoagulants *Proceedings of X World Congress of Cardiology*. Washington: 1986:419 (Abstract 2414)atio

**AMIHOT II , 2000:**

Haude M. AMIHOT-II: A prospective, randomized evaluation of supersaturated oxygen therapy after percutaneous coronary intervention in acute anterior myocardial infarction *Herz* 2007;32 (8):669

Stone GW, Martin JL, de Boer MJ, Margheri M, Bramucci E, Blankenship JC, Metzger DC, Gibbons RJ, Lindsay BS, Weiner BH, Lansky AJ, Krucoff MW, Fahy M, Boscardin WJ Effect of supersaturated oxygen delivery on infarct size after percutaneous coronary intervention in acute myocardial infarction. *Circ Cardiovasc Interv* 2009;2:366-75 [[20031745](#)] [10.1161/CIRCINTERVENTIONS.108.840066](#)

**AMIHOT, 2007:**

O'Neill WW, Martin JL, Dixon SR, Bartorelli AL, Trabattoni D, Oemrawsingh PV, Atsma DE, Chang M, Marquardt W, Oh JK, Krucoff MW, Gibbons RJ, Spears JR Acute Myocardial Infarction with Hyperoxemic Therapy (AMIHOT): a prospective, randomized trial of intracoronary hyperoxemic reperfusion after percutaneous coronary intervention. *J Am Coll Cardiol* 2007;50:397-405 [[17662390](#)] [10.1016/j.jacc.2007.01.099](#)

Stone GW, Martin JL, de Boer MJ, Margheri M, Bramucci E, Blankenship JC, Metzger DC, Gibbons RJ, Lindsay BS, Weiner BH, Lansky AJ, Krucoff MW, Fahy M, Boscardin WJ Effect of supersaturated oxygen delivery on infarct size after percutaneous coronary intervention in acute myocardial infarction. *Circ Cardiovasc Interv* 2009;2:366-75 [[20031745](#)] [10.1161/CIRCINTERVENTIONS.108.840066](#)

**ASPECT-2 (coumadin+asp vs asp), 2002:**

van Es RF, Jonker JJ, Verheugt FW, Deckers JW, Grobbee DE Aspirin and coumadin after acute coronary syndromes (the ASPECT-2 study): a randomised controlled trial. *Lancet* 2002;360:109-13 [[12126819](#)]

**ATACS (Cohen), 1994:**

Cohen M, Adams PC, Parry G, Xiong J, Chamberlain D, Wieczorek I, Fox KA, Chesebro JH, Strain J, Keller C Combination antithrombotic therapy in unstable rest angina and non-Q-wave infarction in nonprior aspirin users. Primary end points analysis from the ATACS trial. *Antithrombotic Therapy in Acute Coronary Syndromes Research Group*. *Circulation* 1994;89:81-8 [[8281698](#)]

**Cohen (ATACS pilot) (heparin+aspirin vs asp), 1990:**

Cohen M, Adams PC, Hawkins L, Bach M, Fuster V Usefulness of antithrombotic therapy in resting angina pectoris or non-Q-wave myocardial infarction in preventing death and myocardial infarction (a pilot study from the Antithrombotic Therapy in Acute Coronary Syndromes Study Group). *Am J Cardiol* 1990;66:1287-92 [[2244556](#)]

**ATACS (pilot study) (warfarin vs control), 1990:**

Cohen M, Adams PC, Hawkins L, Bach M, Fuster V Usefulness of antithrombotic therapy in resting angina pectoris or non-Q-wave myocardial infarction in preventing death and myocardial infarction (a pilot study from the Antithrombotic Therapy in Acute Coronary Syndromes Study Group). *Am J Cardiol* 1990;66:1287-92 [2244556]

**ATACS, 1994:**

Cohen M, Adams PC, Parry G, Xiong J, Chamberlain D, Wieczorek I, Fox KA, Chesebro JH, Strain J, Keller C Combination antithrombotic therapy in unstable rest angina and non-Q-wave infarction in nonprior aspirin users. Primary end points analysis from the ATACS trial. *Antithrombotic Therapy in Acute Coronary Syndromes Research Group. Circulation* 1994;89:81-8 [8281698]

**CARS, 1997:**

Randomised double-blind trial of fixed low-dose warfarin with aspirin after myocardial infarction. Coumadin Aspirin Reinfarction Study (CARS) Investigators. *Lancet* 1997;350:389-96 [9259652]

**OASIS Pilot (phase 1), 1998:**

Anand SS, Yusuf S, Pogue J, Weitz JI, Flather M Long-term oral anticoagulant therapy in patients with unstable angina or suspected non-Q-wave myocardial infarction: organization to assess strategies for ischemic syndromes (OASIS) pilot study results. *Circulation* 1998;98:1064-70 [9736592]

**OASIS Pilot (phase 2), 1998:**

Anand SS, Yusuf S, Pogue J, Weitz JI, Flather M Long-term oral anticoagulant therapy in patients with unstable angina or suspected non-Q-wave myocardial infarction: organization to assess strategies for ischemic syndromes (OASIS) pilot study results. *Circulation* 1998;98:1064-70 [9736592]

**OASIS-2 Warfarin Substudy, 2001:**

Effects of long-term, moderate-intensity oral anticoagulation in addition to aspirin in unstable angina. The Organization to Assess Strategies for Ischemic Syndromes (OASIS) Investigators. *J Am Coll Cardiol* 2001;37:475-84 [11216966]

**APRICOT-2, 2002:**

Brouwer MA, van den Bergh PJ, Aengevaeren WR, Veen G, Luijten HE, Hertzberger DP, van Boven AJ, Vromans RP, Uijen GJ, Verheugt FW Aspirin plus coumarin versus aspirin alone in the prevention of reocclusion after fibrinolysis for acute myocardial infarction: results of the Antithrombotics in the Prevention of Reocclusion In Coronary Thrombolysis (APRICOT)-2 Trial. *Circulation* 2002;106:659-65 [12163424]

**CHAMP, 2002:**

Fiore LD, Ezekowitz MD, Brophy MT, Lu D, Sacco J, Peduzzi P Department of Veterans Affairs Cooperative Studies Program Clinical Trial comparing combined warfarin and aspirin with aspirin alone in survivors of acute myocardial infarction: primary results of the CHAMP study. *Circulation* 2002;105:557-63 [11827919]

**WARIS, 2002:**

Hurlen M, Abdelnoor M, Smith P, Erikssen J, Arnesen H Warfarin, aspirin, or both after myocardial infarction. *N Engl J Med* 2002;347:969-74 [12324552]

**LoWASA, 2004:**

Herlitz J, Holm J, Peterson M, Karlson BW, Haglid Evander M, Erhardt L Effect of fixed low-dose warfarin added to aspirin in the long term after acute myocardial infarction; the LoWASA Study. *Eur Heart J* 2004;25:232-9 [14972424]

**Zibaeenezhad, 2004:**

Zibaeenezhad MJ, Mowla A, Sorbi MH Warfarin and aspirin versus aspirin alone in patients with acute myocardial infarction: a pilot study. *Angiology* 2004;55:17-20 [14759085]

**ACUITY (biva alone vs hep+aGP2b3a), 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 Nov 23;355:2203-16 [17124018]

Singh S, Molnar J, Arora R Efficacy and safety of bivalirudin versus heparins in reduction of cardiac outcomes in acute coronary syndrome and percutaneous coronary interventions. *J Cardiovasc Pharmacol Ther* 2007;12:283-91 [18172222]

Stone GW, Ware JH, Bertrand ME, Lincoff AM, Moses JW, Ohman EM, White HD, Feit F, Colombo A, McLaurin BT, Cox DA, Manoukian SV, Fahy M, Clayton TC, Mehran R, Pocock SJ Antithrombotic strategies in patients with acute coronary syndromes undergoing early invasive management: one-year results from the ACUITY trial. *JAMA* 2007 Dec 5;298:2497-506 [18056903]

**ACUITY (sub groups PCI, bivalirudin alone) import, 2007:**

Stone GW, Ware JH, Bertrand ME, Lincoff AM, Moses JW, Ohman EM, White HD, Feit F, Colombo A, McLaurin BT, Cox DA, Manoukian SV, Fahy M, Clayton TC, Mehran R, Pocock SJ, , Antithrombotic strategies in patients with acute coronary syndromes undergoing early invasive management: one-year results from the ACUTY trial. *JAMA* 2007;298:2497-506. [18056903] [10.1001/jama.298.21.2497](https://doi.org/10.1001/jama.298.21.2497)

Stone GW, White HD, Ohman EM, Bertrand ME, Lincoff AM, McLaurin BT, Cox DA, Pocock SJ, Ware JH, Feit F, Colombo A, Manoukian SV, Lansky AJ, Mehran R, Moses JW, , Bivalirudin in patients with acute coronary syndromes undergoing percutaneous coronary intervention: a subgroup analysis from the Acute Catheterization and Urgent Intervention Triage strategy (ACUTY) trial. *Lancet* 2007;369:907-19. [17368152] [10.1016/S0140-6736\(07\)60450-4](https://doi.org/10.1016/S0140-6736(07)60450-4)

Stone GW, Bertrand M, Colombo A, Dangas G, Farkouh ME, Feit F, Lansky AJ, Lincoff AM, Mehran R, Moses JW, Ohman M, White HD, Acute Catheterization and Urgent Intervention Triage strategy (ACUTY) trial: study design and rationale. *Am Heart J* 2004;148:764-75. [15523305] [10.1016/j.ahj.2004.04.036](https://doi.org/10.1016/j.ahj.2004.04.036)  
**ACUTY (biva+aGP2b3a vs hep+aGP2b3a), 2006:**

Stone GW, Ware JH, Bertrand ME, Lincoff AM, Moses JW, Ohman EM, White HD, Feit F, Colombo A, McLaurin BT, Cox DA, Manoukian SV, Fahy M, Clayton TC, Mehran R, Pocock SJ Antithrombotic strategies in patients with acute coronary syndromes undergoing early invasive management: one-year results from the ACUTY trial. *JAMA* 2007 Dec 5;298:2497-506 [18056903]

**ACUTY (sub groups PCI, bivalirudin +aGP2b3a) import, 2007:**

Stone GW, White HD, Ohman EM, Bertrand ME, Lincoff AM, McLaurin BT, Cox DA, Pocock SJ, Ware JH, Feit F, Colombo A, Manoukian SV, Lansky AJ, Mehran R, Moses JW, , Bivalirudin in patients with acute coronary syndromes undergoing percutaneous coronary intervention: a subgroup analysis from the Acute Catheterization and Urgent Intervention Triage strategy (ACUTY) trial. *Lancet* 2007;369:907-19. [17368152] [10.1016/S0140-6736\(07\)60450-4](https://doi.org/10.1016/S0140-6736(07)60450-4)

**UNASEM, 1992:**

Br FW, Verheugt FW, Col J, Materne P, Monassier JP, Geslin PG, Metzger J, Raynaud P, Foucault J, de Zwaan C Thrombolysis in patients with unstable angina improves the angiographic but not the clinical outcome. Results of UNASEM, a multicenter, randomized, placebo-controlled, clinical trial with anistreplase. *Circulation* 1992;86:131-7 [1617766]

**APPRAISE 2, 2011:**

Alexander JH, Lopes RD, James S, Kilaru R, He Y, Mohan P, Bhatt DL, Goodman S, Verheugt FW, Flather M, Huber K, Liaw D, Husted SE, Lopez-Sendon J, De Caterina R, Jansky P, Darius H, Vinereanu D, Cornel JH, Cools F, Atar D, Leiva-Pons JL, Keltai M, Ogawa H Apixaban with Antiplatelet Therapy after Acute Coronary Syndrome. *N Engl J Med* 2011 Jul 24;: [21780946] [10.1056/NEJMoa1105819](https://doi.org/10.1056/NEJMoa1105819)

**APPRAISE-1 (10mg od), 2009:**

Apixaban, an Oral, Direct, Selective Factor Xa Inhibitor, in Combination With Antiplatelet Therapy After Acute Coronary Syndrome. Results of the Apixaban for Prevention of Acute Ischemic and Safety Events (APPRAISE) Trial. *Circulation* 2009;: [19470889]

**APPRAISE-1 (2.5 mg bid), 2009:**

*Circulation* 2009;: [19470889]

**APPRAISE japan, :**

ongoing trial NCT00852397

**VA-main, 1983:**

Lewis HD Jr, Davis JW, Archibald DG, Steinke WE, Smitherman TC, Doherty JE 3rd, Schnaper HW, LeWinter MM, Linares E, Pouget JM, Sabharwal SC, Chesler E, DeMots H Protective effects of aspirin against acute myocardial infarction and death in men with unstable angina. Results of a Veterans Administration Cooperative Study. *N Engl J Med* 1983;309:396-403 [6135989]

**ISIS-pilot, 1987:**

Randomized factorial trial of high-dose intravenous streptokinase, of oral aspirin and of intravenous heparin in acute myocardial infarction. ISIS (International Studies of Infarct Survival) pilot study. *Eur Heart J* 1987;8:634-42 [2887430]

**ISIS-2, 1988:**

Randomised trial of intravenous streptokinase, oral aspirin, both, or neither among 17,187 cases of suspected acute myocardial infarction: ISIS-2. ISIS-2 (Second International Study of Infarct Survival) Collaborative Group. *Lancet* 1988;2:349-60 [2899772]

**VA-pilot, 0:**

unpublished

Lewis HD *Circulation* 1985;72 (suppl V):155-60

**RISC, 1990:**

Risk of myocardial infarction and death during treatment with low dose aspirin and intravenous heparin in men with unstable coronary artery disease. The RISC Group. *Lancet* 1990;336:827-30 [[1976875](#)]

Wallentin LC Aspirin (75 mg/day) after an episode of unstable coronary artery disease: long-term effects on the risk for myocardial infarction, occurrence of severe angina and the need for revascularization. Research Group on Instability in Coronary Artery Disease in Southeast Sweden. *J Am Coll Cardiol* 1991;18:1587-93 [[1960301](#)]  
**Canadian (Aspirin vs PBO), 1985:**

Cairns JA, Gent M, Singer J, Finnie KJ, Froggatt GM, Holder DA, Jablonsky G, Kostuk WJ, Melendez LJ, Myers MG *N Engl J Med* 1985;313:1369-75 [[3903504](#)]  
**ALDUSA-pilot, 0:**

unpublished

Unit de Pharmacologie Clinique, 1987. (Unit de Pharmacologie Clinique unpublished report)

**Dutch-aspirin, 1990:**

Verheugt FW, van der Laarse A, Funke-Kpper AJ, Sterkman LG, Galema TW, Roos JP Effects of early intervention with low-dose aspirin (100 mg) on infarct size, reinfarction and mortality in anterior wall acute myocardial infarction. *Am J Cardiol* 1990;66:267-70 [[2195861](#)]

**Throux, 1988:**

Theroux P, Ouimet H, McCans J, Latour JG, Joly P, Levy G, Pelletier E, Juneau M, Stasiak J, deGuise P Aspirin, heparin, or both to treat acute unstable angina. *N Engl J Med* 1988 Oct 27;319:1105-11 [[3050522](#)]

**APRICOT, 1993:**

Meijer A, Verheugt FW, Werter CJ, Lie KI, van der Pol JM, van Eenige MJ Aspirin versus coumadin in the prevention of reocclusion and recurrent ischemia after successful thrombolysis: a prospective placebo-controlled angiographic study. Results of the APRICOT Study. *Circulation* 1993;87:1524-30 [[8491007](#)]

**Prandoni, 1991:**

Prandoni P, Milani L, Barbiero M, Cardaioli P, Sanson A, Barbaresi F, Zonzin P, Visani L [Treatment of unstable angina with dipyridamole combined with low doses of aspirin. A multicenter pilot double-blind controlled study] *Minerva Cardioangiol* 1991;39:267-73 [[1780077](#)]

**Canadian (Aspirin + sulfinpyrazone), 1985:**

Cairns JA, Gent M, Singer J, Finnie KJ, Froggatt GM, Holder DA, Jablonsky G, Kostuk WJ, Melendez LJ, Myers MG Aspirin, sulfinpyrazone, or both in unstable angina. Results of a Canadian multicenter trial. *N Engl J Med* 1985;313:1369-75 [[3903504](#)]

**LANCELOT ACS, :**

O'Donoghue ML, Bhatt DL, Wiviott SD, Goodman SG, Fitzgerald DJ, Angiolillo DJ, Goto S, Montalescot G, Zeymer U, Aylward PE, Guetta V, Dudek D, Ziecina R, Contant CF, Flather MD Safety and tolerability of atropaxar in the treatment of patients with acute coronary syndromes: the lessons from antagonizing the cellular effects of ThrombinAcute Coronary Syndromes Trial. *Circulation* 2011 May 3;123:1843-53 [[21502577](#)] [10.1161/CIRCULATIONAHA.110.000786](#)

**J-LANCELOT, 2010:**

**MIRACL, 2001:**

Schwartz GG, Olsson AG, Ezekowitz MD, Ganz P, Oliver MF, Waters D, Zeiher A, Chaitman BR, Leslie S, Stern T Effects of atorvastatin on early recurrent ischemic events in acute coronary syndromes: the MIRACL study: a randomized controlled trial. *JAMA* 2001 Apr 4;285:1711-8 [[11277825](#)]

**REDEEM, 2009:**

unpublished

Oldgren J, Budaj A, Granger CB, Khder Y, Roberts J, Siegbahn A, Tijssen JG, Van de Werf F, Wallentin L Dabigatran vs. placebo in patients with acute coronary syndromes on dual antiplatelet therapy: a randomized, double-blind, phase II trial. *Eur Heart J* 2011 Nov;32:2781-9 [[21551462](#)]

**Gbel (Dutch study), 1995:**

Gobel EJ, Hautvast RW, van Gilst WH, Spanjaard JN, Hillege HL, DeJongste MJ, Molhoek GP, Lie KI Randomised, double-blind trial of intravenous diltiazem versus glyceryl trinitrate for unstable angina pectoris. *Lancet* 1995;346:1653-7 [[8551821](#)]

**DRS, 1986:**

Gibson RS, Boden WE, Theroux P, Strauss HD, Pratt CM, Gheorghide M, Capone RJ, Crawford MH, Schlant RC, Kleiger RE Diltiazem and reinfarction in patients with non-Q-wave myocardial infarction. Results of a double-blind, randomized, multicenter trial. *N Engl J Med* 1986;315:423-9 [[3526151](#)] [10.1056/NEJM198608143150704](#)

**LIPS (sub groups), 2002:**

Serruys PW, de Feyter P, Macaya C, Kokott N, Puel J, Vrolix M, Branzi A, Bertolami MC, Jackson G, Strauss B, Meier B Fluvastatin for prevention of cardiac events following successful first percutaneous coronary intervention: a randomized controlled trial. *JAMA* 2002 Jun 26;287:3215-22 [[12076217](#)]



**FLORIDA, 2002:**

Liem AH, van Boven AJ, Veeger NJ, Withagen AJ, Robles de Medina RM, Tijssen JG, van Veldhuisen DJ Effect of fluvastatin on ischaemia following acute myocardial infarction: a randomized trial. *Eur Heart J* 2002;23:1931-7 [[12473255](#)]

**Czech trial, :**

ongoing trial NCT00171275

**TAUSA, 1994:**

Ambrose JA, Almeida OD, Sharma SK, Torre SR, Marmur JD, Israel DH, Ratner DE, Weiss MB, Hjendahl-Monsen CE, Myler RK Adjunctive thrombolytic therapy during angioplasty for ischemic rest angina. Results of the TAUSA Trial. TAUSA Investigators. Thrombolysis and Angioplasty in Unstable Angina trial. *Circulation* 1994;90:69-77 [[8026054](#)]

**LAMIL, 1997:**

Kesteloot H, Claeys G, Blanckaert N, Lesaffre E Time course of serum lipids and apolipoproteins after acute myocardial infarction: modification by pravastatin. *Acta Cardiol* 1997;52:107-16 [[9187418](#)]

**RECIFE, 1999:**

Dupuis J, Tardif JC, Cernacek P, Throux P Cholesterol reduction rapidly improves endothelial function after acute coronary syndromes. The RECIFE (reduction of cholesterol in ischemia and function of the endothelium) trial. *Circulation* 1999;99:3227-33 [[10385495](#)]

**PAIS, 2001:**

Den Hartog FR, Van Kalmthout PM, Van Loenhout TT, Schaafsma HJ, Rila H, Verheugt FW Pravastatin in acute ischaemic syndromes: results of a randomised placebo-controlled trial. *Int J Clin Pract* 2001;55:300-4 [[11452676](#)]

**PACT, 2004:**

Thompson PL, Meredith I, Amerena J, et al. Effect of pravastatin compared with placebo initiated within 24 hours of onset of acute myocardial infarction or unstable angina: the Pravastatin in Acute Coronary Treatment (PACT) trial *Am Heart J*. 2004;148:e2

Thompson PL, Meredith I, Amerena J, Campbell TJ, Sloman JG, Harris PJ Effect of pravastatin compared with placebo initiated within 24 hours of onset of acute myocardial infarction or unstable angina: the Pravastatin in Acute Coronary Treatment (PACT) trial. *Am Heart J* 2004;148:e2 [[15215811](#)]

**MERLIN TIMI 36, 2007:**

Morrow D Evaluation of a novel anti-ischemic agent in acute coronary syndromes: the primary results of the metabolic efficiency with ranolazine for less ischemia in non-ST elevation acute coronary syndrome (MERLIN)-TIMI 26 trial American College of Cardiology Annual Scientific Session, New Orleans, LA, March 2007

Morrow DA, Scirica BM, Karwatowska-Prokopczuk E, Murphy SA, Budaj A, Varshavsky S, Wolff AA, Skene A, McCabe CH, Braunwald E Effects of ranolazine on recurrent cardiovascular events in patients with non-ST-elevation acute coronary syndromes: the MERLIN-TIMI 36 randomized trial. *JAMA* 2007 Apr 25;297:1775-83 [[17456819](#)]

**ATLAS ACS-TIMI 46 (2.5mg), 2009:**

Mega JL, Braunwald E, Mohanavelu S, Burton P, Poulter R, Misselwitz F, Hricak V, Barnathan ES, Bordes P, Witkowski A, Markov V, Oppenheimer L, Gibson CM Rivaroxaban versus placebo in patients with acute coronary syndromes (ATLAS ACS-TIMI 46): a randomised, double-blind, phase II trial. *Lancet* 2009 Jul 4;374:29-38 [[19539361](#)]

**ATLAS ACS 2 - TIMI 51 (2.5mg), 2011:**

Mega JL, Braunwald E, Wiviott SD, Bassand JP, Bhatt DL, Bode C, Burton P, Cohen M, Cook-Bruns N, Fox KA, Goto S, Murphy SA, Plotnikov AN, Schneider D, Sun X, Verheugt FW, Gibson CM Rivaroxaban in Patients with a Recent Acute Coronary Syndrome. *N Engl J Med* 2011 Nov 13;: [[22077192](#)] [10.1056/NEJMoa1112277](#)

**ATLAS ACS-TIMI 46 (5mg), 2009:**

Mega JL, Braunwald E, Mohanavelu S, Burton P, Poulter R, Misselwitz F, Hricak V, Barnathan ES, Bordes P, Witkowski A, Markov V, Oppenheimer L, Gibson CM Rivaroxaban versus placebo in patients with acute coronary syndromes (ATLAS ACS-TIMI 46): a randomised, double-blind, phase II trial. *Lancet* 2009 Jul 4;374:29-38 [[19539361](#)]

**ATLAS ACS 2 - TIMI 51 (5mg), 2011:**

Mega JL, Braunwald E, Wiviott SD, Bassand JP, Bhatt DL, Bode C, Burton P, Cohen M, Cook-Bruns N, Fox KA, Goto S, Murphy SA, Plotnikov AN, Schneider D, Sun X, Verheugt FW, Gibson CM Rivaroxaban in Patients with a Recent Acute Coronary Syndrome. *N Engl J Med* 2011 Nov 13;: [[22077192](#)] [10.1056/NEJMoa1112277](#)

**A to Z, 2004:**

de Lemos JA, Blazing MA, Wiviott SD, Lewis EF, Fox KA, White HD, Rouleau JL, Pedersen TR, Gardner LH, Mukherjee R, Ramsey KE, Palmisano J, Billheimer DW, Pfeffer MA, Califf RM, Braunwald E Early intensive vs a delayed conservative simvastatin strategy in patients with acute coronary syndromes: phase Z of the A to Z trial. *JAMA* 2004 Sep 15;292:1307-16 [15337732]

**Canadian (sulfinpyrazone alone), 1985:**

Cairns JA, Gent M, Singer J, Finnie KJ, Froggatt GM, Holder DA, Jablonsky G, Kostuk WJ, Melendez LJ, Myers MG *N Engl J Med* 1985;313:1369-75 [3903504]

**Wilcox, 1980:**

Wilcox RG, Richardson D, Hampton JR, Mitchell JR, Banks DC Sulphinpyrazone in acute myocardial infarction: studies on cardiac rhythm and renal function. *Br Med J* 1980;281:531-4 [7000264]

**Louvain sulphinpyrazone, 1983:**

Lijnen P, Boelaert J, van Eeghem P, Daneels R, Schurgers M, de Jaegere P, van der Stichele E, Vincke J, Fagard R, Verschueren LJ, Amery A Decrease in renal function due to sulphinpyrazone treatment early after myocardial infarction. *Clin Nephrol* 1983;19:143-6 [6340878]

**Nicklas, 1989:**

Nicklas JM, Topol EJ, Kander N, O'Neill WW, Walton JA, Ellis SG, Gorman L, Pitt B Randomized, double-blind, placebo-controlled trial of tissue plasminogen activator in unstable angina. *J Am Coll Cardiol* 1989;13:434-41 [2492325]

**Gold, 1987:**

Gold HK, Johns JA, Leinbach RC, Yasuda T, Grossbard E, Zusman R, Collen D A randomized, blinded, placebo-controlled trial of recombinant human tissue-type plasminogen activator in patients with unstable angina pectoris. *Circulation* 1987 Jun;75:1192-9 [3105913]

**Williams, 1990:**

Williams DO, Topol EJ, Califf RM, Roberts R, Mancini GB, Joelson JM, Ellis SG, Kleiman NS Intravenous recombinant tissue-type plasminogen activator in patients with unstable angina pectoris. Results of a placebo-controlled, randomized trial. *Circulation* 1990 Aug;82:376-83 [2115407]

**Freeman, 1992:**

Freeman MR, Langer A, Wilson RF, Morgan CD, Armstrong PW Thrombolysis in unstable angina. Randomized double-blind trial of t-PA and placebo. *Circulation* 1992;85:150-7 [1728444]

**van der Brand, 1991:**

van den Brand M, van Zijl A, Geuskens R, de Feyter PJ, Serruys PW, Simoons ML Tissue plasminogen activator in refractory unstable angina. A randomized double-blind placebo-controlled trial in patients with refractory unstable angina and subsequent angioplasty. *Eur Heart J* 1991;12:1208-14 [1782951]

**Charbonnier, 1992:**

Charbonnier B, Bernadet P, Schiele F, Thery C, Baudouy M, Bauters C [Intravenous thrombolysis by recombinant plasminogen activator (rt-PA) in unstable angina. A randomized multicenter study versus placebo] *Arch Mal Coeur Vaiss* 1992;85:1471-7 [1297297]

**Ardissino, 1990:**

Ardissino D, Barberis P, De Servi S, Mussini A, Rolla A, Visani L, Specchia G Recombinant tissue-type plasminogen activator followed by heparin compared with heparin alone for refractory unstable angina pectoris. *Am J Cardiol* 1990;66:910-4 [2121016]

**TIMI 3B, 1995:**

Anderson HV, Cannon CP, Stone PH, Williams DO, McCabe CH, Knatterud GL, Thompson B, Willerson JT, Braunwald E One-year results of the Thrombolysis in Myocardial Infarction (TIMI) IIIB clinical trial. A randomized comparison of tissue-type plasminogen activator versus placebo and early invasive versus early conservative strategies in unstable angina and non-Q wave myocardial infarction. *J Am Coll Cardiol* 1995;26:1643-50 [7594098]

**Topol, 1988:**

Topol EJ, Nicklas JM, Kander NH, Walton JA, Ellis SG, Gorman L, Pitt B Coronary revascularization after intravenous tissue plasminogen activator for unstable angina pectoris: results of a randomized, double-blind, placebo-controlled trial. *Am J Cardiol* 1988;62:368-71 [2970776]

**TIMI 3A, 1993:**

Early effects of tissue-type plasminogen activator added to conventional therapy on the culprit coronary lesion in patients presenting with ischemic cardiac pain at rest. Results of the Thrombolysis in Myocardial Ischemia (TIMI IIIA) Trial. *Circulation* 1993 Jan;87:38-52 [8419023]



## 11 obesity and overweight

Trial	Treatments	Patients	Trials design and methods
<b>liraglutide vs placebo</b>			
Astrup (NN8022-1807) , 2009 [NCT00422058] n=NA follow-up: 20 weeks	4 liraglutide doses (1.2 mg, 1.8 mg, 2.4 mg, or 3.0 mg daily) versus placebo	obese individuals without type 2 diabetes	Parallel groups double blind Europe
<b>lorcaserin vs placebo</b>			
APD356-004 , 2009 n=NA follow-up:	-	-	
BLOOM , 2010 [NCT00395135] n=NA follow-up: 52 weeks	lorcaserin 10mg bid versus placebo	-	Parallel groups double-blind
BLOOM-DM (10mg bid) <i>unpublished</i> [NCT00603291] n=253/56 follow-up: 52 weeks	lorcaserin 10 mg BID versus placebo	overweight and obese patients with type 2 diabetes mellitus managed with oral hypoglycemic agents	Parallel groups double-blind
BLOSSOM (10mg bid) , 2009 [NCT00603902] n=1603/1603 follow-up: 1 year	lorcaserin 10 mg twice daily versus placebo	obese and overweight patients	Parallel groups double blind USA
<b>Orlistat vs placebo</b>			
Bakris , 2002 n=278/276 follow-up: 1-year	orlistat versus placebo	obese individuals with inadequately controlled hypertension.	double-blind
Broom , 2002 n=265/261 follow-up: 54-week	orlistat versus placebo	obese patients with cardiovascular risk	parallel group double-blind
Broom , 2001 n=71/71 follow-up:	-	-	
Davidson , 1999 n=668/224 follow-up: 52 weeks	orlistat, 120 mg 3 times a day, for 52 weeks versus placebo	Obese adults (BMI 30-43 kg/m2)	double-blind US

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
Deerochanawong , 2001 n=126/126 follow-up:	-	-	
Derosa , 2003 n=27/23 follow-up: 1-year	orlistat 120 mg TID versus placebo	obese patients with hypercholesterolemia	double-blind
Gotfredsen , 2001 n=16/14 follow-up:	-	-	
Halpern , 2003 n=169/174 follow-up: 24 weeks	orlistat (120 mg t.i.d.), versus placebo	Obese, non-insulin-dependent diabetic patients, aged 18-70 years old, with BMI >27 kg/m <sup>2</sup>	parallel Double-blind Latin-America
Hanefeld , 2002 n=195/188 follow-up: 48-week	orlistat 120 mg t.i.d. versus placebo	Overweight or obese adults (BMI ≥ 28 kg/m <sup>2</sup> ) with HbA1c of 6.5-11% and clinical type 2 diabetes	double-blind
Hauptman , 2000 n=210/212 follow-up: 1 year	60 mg of orlistat TID or 120 mg of orlistat TID, versus placebo	obese patients (BMI 30-44 kg/m <sup>2</sup> )	double-blind USA
Hill , 1999 n=181/188 follow-up: 1 year	30 mg orlistat, 60 mg orlistat, or 120 mg orlistat 3 times daily for 1 y versus placebo	Obese subjects who lost ≥ 8% of their initial body weight during a 6-mo lead-in of a prescribed hypoenergetic diet (4180-kJ/d deficit) with no adjunctive pharmacotherapy	double-blind
Hollander , 1998 n=163/159 follow-up: 57-week	120 mg orlistat orally three times a day versus placebo	obese men and women with type 2 diabetes who were aged >18 years, had a BMI of 28-40 kg/m <sup>2</sup> , and were clinically stable on oral sulfonylureas	double-blind
Karhunen , 2000 n=36/36 follow-up: 1 y.	orlistat 120 mg t.i.d. versus placebo	obese subjects	double-blind
Kelley , 2002 n=274/276 follow-up: 1-year	orlistat 120 mg three times a day versus placebo	overweight or obese adults (BMI 28-40 kg/m <sup>2</sup> ) with type 2 diabetes treated with insulin alone or combined with oral agents, but with suboptimal metabolic control (HbA(1c) 7.5-12.0% )	double-blind
Krempf , 2005 n=346/350 follow-up: 18-month	orlistat 120 mg three times daily versus placebo	otherwise healthy, overweight patients aged 18-65 y (BMI ≥ 28 kg/m <sup>2</sup> )	double-blind

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
Lindgarde , 2000 n=190/186 follow-up: 1 year	orlistat 120 mg three times daily versus placebo	obese adults (body mass index 28-38 kg m-2) with type 2 diabetes, hypercholesterolaemia and/or hypertension	double-blind Sweden
Lucas , 2003 n=256/188 follow-up:	-	-	
Micic , 1999 n=60/59 follow-up: 24 weeks	orlistat 120 mg three times daily versus placebo	obese patients (BMI $\geq$ 30 kg/m <sup>2</sup> ) with hyperlipidemia (LDL-cholesterol $\geq$ = 4, 2 mmol/l)	double-blind
Miles , 2002 n=255/261 follow-up: 1 year	120 mg orlistat t.i.d. versus placebo	overweight and obese patients with suboptimal control of type 2 diabetes	double-blind
Muls , 2001 n=147/147 follow-up: 24 week	orlistat 120 mg three times daily versus placebo	obese hypercholesterolemic patients, BMI between 27-40 kg/m <sup>2</sup> and low-density-lipoprotein cholesterol, LDL-C, between 4.1-6.7 mmol/l	double-blind
Naumov , 2002 n=15/15 follow-up:	orlistat versus diet alone	patients with stable angina pectoris concomitant with obesity and hyperlipemia	open
Reaven , 2001 n=156/91 follow-up:	-	-	
Rissanen , 2001 n=25/26 follow-up: 12-month	orlistat 120 mg three times daily versus placebo	healthy obese women	double-blind
Rosenfalck , 2002 n=3/1 follow-up:	-	obese patients	
Rossner , 2000 n=244/243 follow-up: 2-year	orlistat (60 or 120 mg) three times a day versus Obese patients (body mass index 28 to 43 kg/m <sup>2</sup> )	Obese patients (body mass index 28 to 43 kg/m <sup>2</sup> )	double-blind
Shi Yi , 2001 n=986/142 follow-up:	-	-	
Sjostrom , 1998 n=345/343 follow-up: 1 year	-	-	double-blind Europe
Vidgren , 1999 n=37/38 follow-up: 1 year	120 mg of orlistat three times a day versus placebo	obese subjects	
<b>Sibutramine vs placebo</b>			

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
SCOUT , 2010 [NCT00234832] n=4906/4898 follow-up: 3.4 year	sibutramine versus placebo	overweight or obese patients with diabetes or a history of coronary or peripheral vascular disease or stroke, along with other CV risk factors	Parallel groups double blind
McMahon , 2002 n=145/72 follow-up:	-	-	
McMahon , 2000 n=142/157 follow-up:	-	-	
Smith , 2001 n=142/69 follow-up:	-	-	
<b>Topiramate vs placebo</b>			
Bray , 2003 n=75/75 follow-up:	-	-	
Caterson , 2003 n=93/97 follow-up:	-	-	
Pudhomme , 2003 n=33/33 follow-up:	-	-	
Rissanen , 2003 n=123/103 follow-up:	-	-	
Stenlof , 2003 n=135/137 follow-up:	-	-	
Tonstad , 2003 n=178/177 follow-up:	-	-	

More details and results :

- All mechanism for obesity and overweight in all type of patients at <http://www.trialresultscenter.org/go-Q265>

## References

### Astrup (NN8022-1807 ), 2009:

Astrup A, Rssner S, Van Gaal L, Rissanen A, Niskanen L, Al Hakim M, Madsen J, Rasmussen MF, Lean ME Effects of liraglutide in the treatment of obesity: a randomised, double-blind, placebo-controlled study. Lancet 2009 Oct 22;: [19853906] [10.1016/S0140-6736\(09\)61375-1](https://doi.org/10.1016/S0140-6736(09)61375-1)

### APD356-004, 2009:

Smith SR, Prosser WA, Donahue DJ, Morgan ME, Anderson CM, Shanahan WR Lorcaserin (APD356), a selective 5-HT(2C) agonist, reduces body weight in obese men and women. Obesity (Silver Spring) 2009;17:494-503 [19057523] [10.1038/oby.2008.537](https://doi.org/10.1038/oby.2008.537)

**BLOOM, 2010:**

Smith SR, Weissman NJ, Anderson CM, Sanchez M, Chuang E, Stubbe S, Bays H, Shanahan WR Multicenter, Placebo-Controlled Trial of Lorcaserin for Weight Management. *N Engl J Med* 2010 Jul 15;363:245-256 [[20647200](#)] [10.1056/NEJMoa0909809](#)

**BLOOM-DM (10mg bid), :**

unpublished

**BLOSSOM (10mg bid), 2009:**

Kaplan LM, Smith SR, Weissman NJ, et al The BLOSSOM trial: efficacy and safety of lorcaserin in obese and overweight men and women *Obesity* 2009; October 27, 2009; Washington, DC

Fidler MC, Sanchez M, Raether B, Weissman NJ, Smith SR, Shanahan WR, Anderson CM A one-year randomized trial of lorcaserin for weight loss in obese and overweight adults: the BLOSSOM trial. *J Clin Endocrinol Metab* 2011;96:3067-77 [[21795446](#)] [10.1210/jc.2011-1256](#)

**Bakris, 2002:**

Bakris G, Calhoun D, Egan B, Hellmann C, Dolker M, Kingma I Orlistat improves blood pressure control in obese subjects with treated but inadequately controlled hypertension. *J Hypertens* 2002 Nov;20:2257-67 [[12409965](#)]

**Broom, 2002:**

Broom I, Wilding J, Stott P, Myers N Randomised trial of the effect of orlistat on body weight and cardiovascular disease risk profile in obese patients: UK Multimorbidity Study. *Int J Clin Pract* 2002 Sep;56:494-9 [[12296610](#)]

**Broom,, 2001:**

Broom I. Randomised trial of the effect of orlistat on body weight and CVD risk profile in overweight and obese patients with co-morbidities [Abstract]. *Int J Obes.* 2001;25 Suppl:S106

**Davidson, 1999:**

Davidson MH, Hauptman J, DiGirolamo M, Foreyt JP, Halsted CH, Heber D, Heimburger DC, Lucas CP, Robbins DC, Chung J, Heymsfield SB Weight control and risk factor reduction in obese subjects treated for 2 years with orlistat: a randomized controlled trial. *JAMA* 1999 Jan 20;281:235-42 [[9918478](#)]

**Deerochanawong,, 2001:**

Deerochanawong C. Effect of treatment with orlistat in overweight or obese Thai patients with type 2 diabetes [Abstract]. *Diabetes.* 2001;50:A433.

**Derosa, 2003:**

Derosa G, Mugellini A, Ciccarelli L, Fogari R Randomized, double-blind, placebo-controlled comparison of the action of orlistat, fluvastatin, or both an anthropometric measurements, blood pressure, and lipid profile in obese patients with hypercholesterolemia prescribed a standardized diet. *Clin Ther* 2003 Apr;25:1107-22 [[12809960](#)]

**Gotfredsen, 2001:**

Reaven G, Segal K, Hauptman J, Boldrin M, Lucas C Effect of orlistat-assisted weight loss in decreasing coronary heart disease risk in patients with syndrome X. *Am J Cardiol* 2001 Apr 1;87:827-31 [[11274935](#)]

**Halpern, 2003:**

Halpern A, Mancini MC, Suplicy H, Zanella MT, Repetto G, Gross J, Jadzinsky M, Barranco J, Aschner P, Ramirez L, Matos AG Latin-American trial of orlistat for weight loss and improvement in glycaemic profile in obese diabetic patients. *Diabetes Obes Metab* 2003 May;5:180-8 [[12681025](#)]

**Hanefeld, 2002:**

Hanefeld M, Sachse G The effects of orlistat on body weight and glycaemic control in overweight patients with type 2 diabetes: a randomized, placebo-controlled trial. *Diabetes Obes Metab* 2002 Nov;4:415-23 [[12406041](#)]

**Hauptman, 2000:**

Hauptman J, Lucas C, Boldrin MN, Collins H, Segal KR Orlistat in the long-term treatment of obesity in primary care settings. *Arch Fam Med* 2000 Feb;9:160-7 [[10693734](#)]

**Hill, 1999:**

Hill JO, Hauptman J, Anderson JW, Fujioka K, O'Neil PM, Smith DK, Zavoral JH, Aronne LJ Orlistat, a lipase inhibitor, for weight maintenance after conventional dieting: a 1-y study. *Am J Clin Nutr* 1999 Jun;69:1108-16 [[10357727](#)]

**Hollander, 1998:**

Hollander PA, Elbein SC, Hirsch IB, Kelley D, McGill J, Taylor T, Weiss SR, Crockett SE, Kaplan RA, Comstock J, Lucas CP, Lodewick PA, Canovatchel W, Chung J, Hauptman J Role of orlistat in the treatment of obese patients with type 2 diabetes. A 1-year randomized double-blind study. *Diabetes Care* 1998 Aug;21:1288-94 [9702435]

**Karhunen, 2000:**

Karhunen L, Franssila-Kallunki A, Rissanen P, Valve R, Kolehmainen M, Rissanen A, Uusitupa M Effect of orlistat treatment on body composition and resting energy expenditure during a two-year weight-reduction programme in obese Finns. *Int J Obes Relat Metab Disord* 2000 Dec;24:1567-72 [11126207]

**Kelley, 2002:**

Kelley DE, Bray GA, Pi-Sunyer FX, Klein S, Hill J, Miles J, Hollander P Clinical efficacy of orlistat therapy in overweight and obese patients with insulin-treated type 2 diabetes: A 1-year randomized controlled trial. *Diabetes Care* 2002 Jun;25:1033-41 [12032111]

**Krempf, 2005:**

Krempf M, Louvet JP, Allanic H, Miloradovich T, Joubert JM, Attali JR Weight reduction and long-term maintenance after 18 months treatment with orlistat for obesity. *Int J Obes Relat Metab Disord* 2003 May;27:591-7 [12704403]

**Lindgarde, 2000:**

Lindgarde F The effect of orlistat on body weight and coronary heart disease risk profile in obese patients: the Swedish Multimorbidity Study. *J Intern Med* 2000 Sep;248:245-54 [10971792]

**Lucas, 2003:**

Lucas CP, Boldrin MN, Reaven GM Effect of orlistat added to diet (30

**Micic, 1999:**

Micic D, Ivkovic-Lazar T, Dragojevic R, Jorga J, Stokic E, Hajdukovic Z Orlistat, a gastrointestinal lipase inhibitor, in therapy of obesity with concomitant hyperlipidemia. *Med Pregl* 1999 Sep-Oct;52:323-33 [10624380]

**Miles, 2002:**

Miles JM, Leiter L, Hollander P, Wadden T, Anderson JW, Doyle M, Foreyt J, Aronne L, Klein S Effect of orlistat in overweight and obese patients with type 2 diabetes treated with metformin. *Diabetes Care* 2002 Jul;25:1123-8 [12087008]

**Muls, 2001:**

Muls E, Kolanowski J, Scheen A, Van Gaal L The effects of orlistat on weight and on serum lipids in obese patients with hypercholesterolemia: a randomized, double-blind, placebo-controlled, multicentre study. *Int J Obes Relat Metab Disord* 2001 Nov;25:1713-21 [11753595]

**Naumov, 2002:**

Naumov VG, Lupanov VP, Dotsenko IuV, Tvorogova MG [Six-month xenical (orlistat) therapy of patients with stable angina pectoris concomitant with obesity and hyperlipidemia] *Ter Arkh* 2002;74:47-51 [11878059]

**Reaven, 2001:**

Reaven G, Segal K, Hauptman J, Boldrin M, Lucas C Effect of orlistat-assisted weight loss in decreasing coronary heart disease risk in patients with syndrome X. *Am J Cardiol* 2001 Apr 1;87:827-31 [11274935]

**Rissanen, 2001:**

Rissanen P, Vahtera E, Krusius T, Uusitupa M, Rissanen A Weight change and blood coagulability and fibrinolysis in healthy obese women. *Int J Obes Relat Metab Disord* 2001 Feb;25:212-8 [11410822]

**Rosenfalck, 2002:**

Rosenfalck AM, Hendel H, Rasmussen MH, Almdal T, Anderson T, Hilsted J, Madsbad S Minor long-term changes in weight have beneficial effects on insulin sensitivity and beta-cell function in obese subjects. *Diabetes Obes Metab* 2002 Jan;4:19-28 [11890163]

**Rossner, 2000:**

Rossner S, Sjostrom L, Noack R, Meinders AE, Noseda G Weight loss, weight maintenance, and improved cardiovascular risk factors after 2 years treatment with orlistat for obesity. *European Orlistat Obesity Study Group. Obes Res* 2000 Jan;8:49-61 [10678259]

**Shi Yi, 2001:**

Shi Yi F, Zhu Jun R. Effect of orlistat on weight loss and glycemic control in overweight Chinese patients with type 2 diabetes [Abstract]. *Diabetes*. 2001;50:A101-A102

**Sjostrom, 1998:**

Sjostrom L, Rissanen A, Andersen T, Boldrin M, Golay A, Koppeschaar HP, Krempf M Randomised placebo-controlled trial of orlistat for weight loss and prevention of weight regain in obese patients. European Multicentre Orlistat Study Group. *Lancet* 1998 Jul 18;352:167-72 [9683204]

**Vidgren, 1999:**

Vidgren HM, Agren JJ, Valve RS, Karhunen LJ, Rissanen AM, Uusitupa MI The effect of orlistat on the fatty acid composition of serum lipid fractions in obese subjects. *Clin Pharmacol Ther* 1999 Sep;66:315-22 [10511068]

**SCOUT, 2010:**

James W. P. T. The SCOUT study: risk-benefit profile of sibutramine in overweight high-risk cardiovascular patients *Eur Heart J Suppl* 2005;7:L44-48

Torp-Pedersen C, Caterson I, Coutinho W, Finer N, Van Gaal L, Maggioni A, Sharma A, Brisco W, Deaton R, Shepherd G, James P Cardiovascular responses to weight management and sibutramine in high-risk subjects: an analysis from the SCOUT trial. *Eur Heart J* 2007 Dec;28:2915-23 [17595194]

James WP, Caterson ID, Coutinho W, Finer N, Van Gaal LF, Maggioni AP, Torp-Pedersen C, Sharma AM, Shepherd GM, Rode RA, Renz CL Effect of sibutramine on cardiovascular outcomes in overweight and obese subjects. *N Engl J Med* 2010 Sep 2;363:905-17 [20818901] 10.1056/NEJMoa1003114

**McMahon, 2002:**

McMahon FG, Weinstein SP, Rowe E, Ernst KR, Johnson F, Fujioka K Sibutramine is safe and effective for weight loss in obese patients whose hypertension is well controlled with angiotensin-converting enzyme inhibitors. *J Hum Hypertens* 2002 Jan;16:5-11 [11840224]

**McMahon, 2000:**

McMahon FG, Fujioka K, Singh BN, Mendel CM, Rowe E, Rolston K, Johnson F, Mooradian AD Efficacy and safety of sibutramine in obese white and African American patients with hypertension: a 1-year, double-blind, placebo-controlled, multicenter trial. *Arch Intern Med* 2000 Jul 24;160:2185-91 [10904462]

**Smith, 2001:**

Smith IG, Goulder MA Randomized placebo-controlled trial of long-term treatment with sibutramine in mild to moderate obesity. *J Fam Pract* 2001 Jun;50:505-12 [11407998]

**Bray, 2003:**

Bray GA, Hollander P, Klein S, Kushner R, Levy B, Fitchet M, Perry BH A 6-month randomized, placebo-controlled, dose-ranging trial of topiramate for weight loss in obesity. *Obes Res* 2003 Jun;11:722-33 [12805393]

**Caterson, 2003:**

Caterson I, Astrup A, Zelissen P, Guy-Grand B, Carruba M, Levy B, et al. The long-term effect of topiramate on body weight maintenance after low-calorie diet-induced weight loss in obese subjects [Abstract]. Presented at the 18th International Diabetes Federation Congress, Paris, France, 2429 August 2003.

**Pudhomme, 2003:**

**Rissanen, 2003:**

**Stenlof, 2003:**

**Tonstad, 2003:**

## 12 thrombosis prevention

Trial	Treatments	Patients	Trials design and methods
<b>IPC + aspirin vs aspirin</b>			
Hull 2 (+asp) , 1979 n=NA follow-up:	-	patients undergoing elective knee surgery	open
Hull (+asp) , 1979 n=NA follow-up:	-	patients undergoing elective knee surgery	Parallel groups open

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
65279;Lieberman (A) , 1994 n=130/130 follow-up:	hypotensive epidural anesthesia, external pneumatic-compression boots, and aspirin versus hypotensive epidural anesthesia and aspirin	primary unilateral or bilateral total hip arthroplasty with use of hypotensive epidural anesthesia	Parallel groups open
<b>aspirin vs control</b>			
Clagett , 1975 n=56/49	A1300 versus control	-	open
Zekert VI , 1982 n=50/50	A1500 versus control	-	open
<b>aspirin + dipyridamol vs control</b>			
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
<b>certoparin vs control</b>			
Kock , 1995 n=176/163 follow-up: 15 days	Certoparin 3000 IU versus no prophylaxis	patients with minor injuries treated with plaster-cast immobilisation of the leg	Parallel groups open
<b>deltaparin vs control</b>			
Michot , 2002 n=66/64 follow-up: 30 days	deltaparin 2500IU 60-120min before procedure, followed 6hrs after the end of the procedure by 2500IU (<70kg) or 5000 IU(>70kg) versus no treatment	patients requiring diagnostic or therapeutic arthroscopic knee surgery as outpatients; aged 18 to 80 years.	Parallel groups open Switzerland.
<b>dipyridamol + aspirin vs control</b>			
Parodi I , 1973 n=40/22	Dip,A1000+Dip versus control	-	open
Parodi II , 1973 n=91/35	A1500,Dip,A+Dip versus control	-	open
Australian I , 1975 n=75/75	A1000+Dip versus control	-	open
Australian II , 1976 n=85/75	A1000+Dip versus control	-	open

continued...



<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
Toulouse I , 1979 n=38/66	A990+Dip versus control	-	open
Zekert-III , 1977 n=135/46	A1500,A1300+Dip,A1000+Dip versus control	-	open
Harjola DVT , 1982 n=300/100	A1500,Dip,A+Dip versus control	-	open
Weiss , 1977 n=30/36	A990+Dip versus control	-	open
<b>enoxaparin vs control</b>			
Canata , 2003 n=18/18 follow-up: 6 days	enoxaparin sc daily (dose not specified) versus no treatment	ACL reconstruction for symptomatic ACL-deficient knees	Parallel groups Italy
<b>Footpump (monotherapy) vs control</b>			
Scurr , 1981 n=33/33 follow-up:	Plantar flexion and dorsiflexion of the feet while the patient is on the operating table by the use of a mechanical device (the Pedi-Pulsor) versus control	abdominal or thoracic surgery	open
Wilson , 1992 n=28/32	-	Elective knee replacement	open
<b>IPC sequential compression vs control</b>			
65279;Blackshear excluder , 1987 n=20/20 follow-up:	Sequential external pneumatic compression versus control	abdominal or thoracic surgery	Cross over open
Hull II , 1990 n=152/158 follow-up:	sequential intermittent calf and thigh compression versus no prophylaxis	patients undergoing total hip replacement	open
Fisher , 1995 n=145/159 follow-up:	pneumatic sequential leg compression devices versus no specific form of prophylaxis	orthopaedic trauma patients with hip and pelvic fractures	Parallel groups open
Turple II , 1979 n=112/106 follow-up:	-	patients with intracranial disease	open

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>Knudson , 1994</b> n=26/39 follow-up:	sequential gradient pneumatic leg compression versus control	trauma patients	open
<b>Kosir , 1996</b> n=25/45 follow-up: 30 days	sequential pneumatic compression devices during surgery and 2 days postoperatively versus control	Patients undergoing procedures of at least 1 hr duration (abdominal, thoracic, head and neck, inguinal) requiring general or spinal anesthetic	Parallel groups open
<b>nadroparin vs control</b>			
<b>KANT (7 days) , 2008</b> n=657/660 follow-up: 3 months	once-daily subcutaneous injection of LMWH (nadroparin, 3800 anti-Xa IU) for 7 days versus full-length graduated compression stocking for 7 days	patients undergoing knee arthroscopy	Parallel groups open (blinded assessment) Italy
<b>Roth , 1995</b> n=61/61 follow-up: 4 days	0.3 ml sc fraxiparine 2 hours before the operation and self administered daily (except the first two doses) for 4 days after surgery n/x versus no treatment	patients undergoing ambulatory arthroscopic	Parallel groups Germany
<b>Kujath , 1993</b> n=126/126 follow-up: 65279;16 days	Nadroparin 2850 IU versus no prophylaxis	patients with injuries of the lower limb immobilized by a plaster cast	Parallel groups open
<b>nadroparin 14d vs control</b>			
<b>KANT (14 days) , 2008</b> n=444/660 follow-up: 3 months	once-daily subcutaneous injection of LMWH (nadroparin, 3800 anti-Xa IU) for 14 days versus full-length graduated compression stocking for 7 days	patients undergoing knee arthroscopy	Parallel groups open (blinded assessment) Italy
<b>reviparin vs control</b>			
<b>Wirth , 2001</b> n=117/122 follow-up: 7-10 days	reviparin 1,750 anti Xa IU Sc once daily for 7-10 days versus no treatment	elective knee arthroscopy	Parallel groups open (blind assesement) Germany
<b>tinzaparin vs control</b>			
<b>Jorgensen , 2002</b> n=99/106 follow-up: 38 days	Tinzaparin 3500 IU versus no prophylaxis	patients over 18 years of age with planned plaster cast on a lower extremity of at least 3 weeks	Parallel groups open, assessor-blinded
<b>IPC + dextran vs dextran</b>			

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>Smith (D) , 1978</b> n=97/97 follow-up:	dextran 70 and pneumatic calf compression versus dextran 70	-	open
<b>betrixaban vs enoxaparin</b>			
<b>APEX , 2016</b> [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
<b>nadroparin vs enoxaparin</b>			
<b>FX140, Simonneau G , 2006</b>  n=NA follow-up:	-	-	
<b>semuloparin vs enoxaparin</b>			
<b>SAVE-HIP1 , 2012</b> [NCT00697099] n=1161/1165 follow-up:	Semuloparin 20 mg once-daily versus Enoxaparin 40 mg once-daily	-	
<b>SAVE-KNEE , 2012</b> [NCT00718224] n=576/574 follow-up:	Semuloparin 20 mg once-daily versus Enoxaparin 30 mg twice-daily	-	
<b>SAVE-HIP 2 , 2012</b> [NCT00721760] n=500/503 follow-up:	Semuloparin 20 mg once-daily versus Enoxaparin 40 mg once-daily	hip fracture surgery	Parallel groups
<b>Extended-duration prophylaxis vs error</b>			
<b>EXCLAIM , 2010</b> [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
<b>IPC sequential compression vs Footpump</b>			
<b>Elliott , 1999</b> n=149 follow-up: NA	Calf-thigh sequential pneumatic compression versus foot pump (plantar venous pneumatic compression)	Trauma patients >13 years old	Parallel groups open (blind assesment) United States
<b>CECT + aspirin vs LMWH</b>			

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>Gelfer , 2006</b> n=NA follow-up: 8 days	continuous enhanced circulation therapy (CECT) combined with low-dose aspirin versus enoxaparin 40 mg daily	patients who underwent total hip or knee arthroplasty	Parallel groups open
<b>Aspirin vs no treatment</b>			
<b>Pasteyer , 1977</b> n=20/20 follow-up: 2 weeks	Aspirin 1000mg daily + Hep versus control (Hep alone)	Elective orthopaedic surgery	Parallel groups
<b>Rocha , 1986</b> n=60/30 follow-up: 1 weeks	Aspirin 250mg or 1000mg daily versus control (combination of heparin plus dihydroergotamine)	total hip replacement	Parallel groups open
<b>aspirin + dipyridamol vs no treatment</b>			
<b>Morris-B , 1977</b> n=32/32 follow-up:	Aspirin 900 mg daily + dipyridamole versus control	elderly patients with hip fractures	Parallel groups open
<b>Lyon-I , 1975</b> n=20/20 follow-up: 2 weeks	Aspirin 1500 mg daily + Dipyridamole versus control	Elective orthopaedic surgery	
<b>dipyridamol vs no treatment</b>			
<b>Morris-A , 1977</b> n=24/24 follow-up:	dipyridamole versus control	elderly patients with hip fractures	Parallel groups open
<b>enoxaparin vs no treatment</b>			
<b>Ho [43]</b> n=134/169	Enoxaparin 4000 anti-Xa units versus No treatment	-	Open
<b>Warwick , 1995</b> n=78/78 follow-up: 8-10 days	enoxaparin 4000x1 + elastic stockings versus no treatment + elastic stockings	Elective hip	open
<b>nadroparin vs no treatment</b>			
<b>Marassi [41]</b> n=31/33	Nadroparin 2850 anti-Xa units versus No treatment	-	Open
<b>Yoo , 1997</b> n=50/50 follow-up: 10 days	nadroparin 41/kgx1 days 1-3, 62/kg x1 days 4-11+elastic stockings versus no treatment	Elective hip	open
<b>PROTECT (nadroparin) ongoing</b> [NCT00881088] n=NA follow-up: 6 weeks	nadroparin 0,3 cc daily during immobilization versus no treatment	patients with a nonsurgical fracture of the lower extremity requiring immobilisation in a below-knee plaster cast	Parallel groups single blind

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>Warfarin vs no treatment</b>			
Pinto , 1970 n=25/25 follow-up: >3 weeks	Warfarin versus No treatment	Hip surgery	Open
Hume , 1973 n=17/19 follow-up: Discharge	Warfarin versus No treatment	THR	Open
Morris , 1976 n=80/80 follow-up: 3 months	Warfarin versus No treatment	HFS	Open
Powers , 1989 n=65/63 follow-up: 3 months	Warfarin versus No treatment	HFS	Open
<b>ardeparin vs placebo</b>			
Levine , 1996 n=122/124 follow-up: 14 days	ardeparin 50/kgx2 +elastic stockings versus Placebo+elastic stockings	Knee	double blind
<b>aspirin vs placebo</b>			
MRC , 1972 n=153/150	A600 versus placebo	general surgery	double-blind
Loew DVT , 1974 n=702/679	A600 versus Placebo	-	double-blind
Erfurt-A , 1979 n=357/357	A1500 versus Placebo	-	double-blind
Zekert V , 1980 n=50/49	A1500+Hep???	-	double-blind
Vinazzer I , 1980 n=402/404	A1500+Hep v Hep versus Placebo	-	double-blind
Vinazzer II , 1977 n=62/62	A1000+Hepv Hep versus Placebo	-	double-blind
Zekert-I , 1974 n=138/140 follow-up:	Aspirin 1500mg daily versus placebo	patients undergoing surgery of hip-joint proximal fractures	Parallel groups double-blind
Powers , 1976 n=66/63	A1300 versus placebo	traumatic orthopaedic surgery	

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>Erfurt-B , 1979</b> n=44/44 follow-up:	A1500 versus placebo	traumatic orthopaedic surgery	double-blind
<b>PEP hip-fracture , 2000</b> n=6679/6677 follow-up: 35 days	aspirin 160mg/d started preoperatively and continued for 35 days versus placebo	patients undergoing surgery for hip fracture	Parallel groups Double blind Australia, New Zealand, South Africa,
<b>PEP elective arthroplasty , 2000</b> n=2047/2041 follow-up: 35 days	aspirin 160mg/d started preoperatively and continued for 35 daysA versus placebo	Patients undergoing elective hip or knee arthroplasty	Parallel groups Double blind New Zealand
<b>Stockholm-I , 1975</b> n=26/25 follow-up: 2 weeks	Aspirin 2000mg daily versus placebo	elective surgery of the hip	double blind
<b>Harris-I , 1977</b> n=58/59 follow-up: 1 weeks	Aspirin 1200mg daily versus placebo	patients over 40 years of age, who had undergone total hip replacement	Parallel groups double-blind
<b>McKenna-I , 1980</b> n=24/12 follow-up: 2 weeks	Aspirin 975mg or 3900mg daily versus placebo	total knee replacement	Parallel groups double-blind
<b>Sautter , 1983</b> n=68/77 follow-up: 3 weeks	Aspirin 900mg daily + sulfinpyrazone versus placebo	patient with total hip replacement	Parallel groups
<b>McBride , 1983</b> n=21/22 follow-up: 1 weeks	A1800+Dipyridamole versus placebo	Elective orthopaedic surgery	
<b>aspirin + dipyridamol vs placebo</b>			
<b>Encke-II , 1976</b> n=34/25 follow-up:	Aspirin 1500mg daily, Aspirin 990mg daily + dipyridamol versus placebo	patients with abdominal operations	Parallel groups double-blind
<b>Hamburg , 1976</b> n=21/11 follow-up: 3 weeks	A+Dipyridamole,A1000 versus placebo	Elective orthopaedic surgery	
<b>Frankfurt , 1981</b> <i>unpublished</i> n=25/14 follow-up:	A+Dip,A1320 versus placebo	patients with myocardial infarction	Parallel groups double-blind
<b>dalteparin vs placebo</b>			
<b>D-KAf (Selby) , 2007</b> [NCT00187408] n=134/131 follow-up:	dalteparin 5000U daily versus placebo	below-knee fractures repaired surgically	

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
Leizorovicz , 2004 n=1856/1850 follow-up: 21 days	Dalteparin 5000E once daily, 1 <sup>st</sup> days versus placebo	Congestive heart failure (NYHA IIIIV), acute or chronic respiratory disease, infectious and rheumatologic disease	Parallel groups double blind
Jorgensen , 1989 n=30/38 follow-up: 9 days	dalteparin 5000 x1 versus Placebo	Hip fracture	double blind
Torholm , 1991 n=58/54 follow-up: 9 days	dalteparin 5000x1 versus Placebo	Elective hip	double blind
Ockelford , 1989 n=102/95	Dalteparin 2500 anti-Xa units versus Placebo	general surgery	Blind
Lapidus , 2007 n=47/44 follow-up: 43 days	Dalteparin 5000 IU versus Placebo	patients surgically treated for Achilles tendon rupture	Parallel groups double-blind
Lapidus , 2007 n=101/96 follow-up: 44 days	Dalteparin 5000 IU versus Placebo	patients undergoing ankle fracture surgery	Parallel groups double-blind

More details and results :

- antithrombotics for thrombosis prevention in orthopedic surgery at <http://www.trialresultscenter.org/go-Q37>
- antithrombotics for thrombosis prevention in elective major knee surgery at <http://www.trialresultscenter.org/go-Q38>
- antithrombotics for thrombosis prevention in elective hip replacement at <http://www.trialresultscenter.org/go-Q39>
- antithrombotics for thrombosis prevention in hip Fracture at <http://www.trialresultscenter.org/go-Q40>
- antithrombotics for thrombosis prevention in medical patients at <http://www.trialresultscenter.org/go-Q87>
- antithrombotics for thrombosis prevention in general surgery at <http://www.trialresultscenter.org/go-Q92>
- antithrombotics for thrombosis prevention in urologic surgery at <http://www.trialresultscenter.org/go-Q93>
- antithrombotics for thrombosis prevention in gynaecological surgery at <http://www.trialresultscenter.org/go-Q94>
- antithrombotics for thrombosis prevention in abdominal surgery at <http://www.trialresultscenter.org/go-Q96>
- antithrombotics for thrombosis prevention in neurosurgery at <http://www.trialresultscenter.org/go-Q99>
- antithrombotics for thrombosis prevention in arthroscopy at <http://www.trialresultscenter.org/go-Q150>
- graduated compression stockings for thrombosis prevention in all type of patients at <http://www.trialresultscenter.org/go-Q158>
- anticoagulant for thrombosis prevention in orthopedic surgery at <http://www.trialresultscenter.org/go-Q184>
- direct antithrombins for thrombosis prevention in orthopedic surgery at <http://www.trialresultscenter.org/go-Q185>
- antiplatelets drug for thrombosis prevention in orthopedic surgery at <http://www.trialresultscenter.org/go-Q186>
- pentasaccharide for thrombosis prevention in orthopedic surgery at <http://www.trialresultscenter.org/go-Q188>
- heparin (UFH or LMWH) for thrombosis prevention in orthopedic surgery at <http://www.trialresultscenter.org/go-Q189>
- LMWH for thrombosis prevention in orthopedic surgery at <http://www.trialresultscenter.org/go-Q190>
- UFH for thrombosis prevention in urologic surgery at <http://www.trialresultscenter.org/go-Q194>
- heparin (UFH or LMWH) for thrombosis prevention in general surgery at <http://www.trialresultscenter.org/go-Q195>

## References

### **Hull 2 (+asp), 1979:**

Hull R, Delmore TJ, Hirsh J, Gent M, Armstrong P, Lofthouse R, MacMillan A, Blackstone I, Reed-Davis R, Detwiler RC Effectiveness of intermittent pulsatile elastic stockings for the prevention of calf and thigh vein thrombosis in patients undergoing elective knee surgery. *Thromb Res* 1979;16:37-45 [505427]

### **Hull (+asp), 1979:**

Hull R, Delmore TJ, Hirsh J, Gent M, Armstrong P, Lofthouse R, MacMillan A, Blackstone I, Reed-Davis R, Detwiler RC Effectiveness of intermittent pulsatile elastic stockings for the prevention of calf and thigh vein thrombosis in patients undergoing elective knee surgery. *Thromb Res* 1979;16:37-45 [505427]

### **65279;Lieberman (A), 1994:**

Lieberman JR, Huo MM, Hanway J, Salvati EA, Sculco TP, Sharrock NE The prevalence of deep venous thrombosis after total hip arthroplasty with hypotensive epidural anesthesia. *J Bone Joint Surg Am* 1994;76:341-8 [8126039]

### **Clagett, 1975:**

Clagett GP, Schneider P, Rosoff CB, Salzman EW The influence of aspirin on postoperative platelet kinetics and venous thrombosis. *Surgery* 1975;77:61-74 [1109518]

### **Zekert VI, 1982:**

Zekert F, Schemper M, Neumann K Acetylsalicylic acid in combination with dihydroergotamine for preventing thromboembolism. *Haemostasis* 1982;11:149-53 [7095604]

### **Chicago, 1982:**

Green D, Rossi EC, Yao JS, Flinn WR, Spies SM Deep vein thrombosis in spinal cord injury: effect of prophylaxis with calf compression, aspirin, and dipyridamole. *Paraplegia* 1982;20:227-34 [6813814]

### **Kock, 1995:**

Kock HJ, Schmit-Neuerburg KP, Hanke J, Rudofsky G, Hirche H Thromboprophylaxis with low-molecular-weight heparin in outpatients with plaster-cast immobilisation of the leg. *Lancet* 1995;346:459-61 [7637478]

### **Michot, 2002:**

Michot M, Conen D, Holtz D, Erni D, Zumstein MD, Ruffin GB, Renner N Prevention of deep-vein thrombosis in ambulatory arthroscopic knee surgery: A randomized trial of prophylaxis with low-molecular weight heparin. *Arthroscopy* 2002;18:257-63 [11877611]

### **Parodi I, 1973:**

Parodi JC, Grandi A, Font E, Rotondaro D, Iorio J, Manrique J. El dipiridamol y el acido acetilsalicilico en la profilaxis de las trombosis venosas postoperatorias de los miembros inferiores *Dia Med* 1973;45:92-3.

### **Parodi II, 1973:**

Parodi JC, Grandi A, Font E, Rotondaro D, Iorio J, Manrique J. El dipiridamol y el acido acetilsalicilico en la profilaxis de las trombosis venosas postoperatorias de los miembros inferiores *Dia Med* 1973;45:92-3.

### **Australian I, 1975:**

O'Sullivan EF, Renney JT. Antiplatelet drugs in the prevention of postoperative deep vein thrombosis In: Proceedings of III congress of Interiational Societyfor Thrombosis andHaemnostasis (Washington). 1972:438.

### **Australian II, 1976:**

Renney JT, O'Sullivan EF, Burke PF Prevention of postoperative deep vein thrombosis with dipyridamole and aspirin. *Br Med J* 1976;1:992-4 [773495]

### **Toulouse I, 1979:**

Plante J, Boneu B, Vaysse C, Barret A, Gouzi M, Bierme R Dipyridamole-aspirin versus low doses of heparin in the prophylaxis of deep venous thrombosis in abdominal surgery. *Thromb Res* 1979;14:399-403 [442014]

### **Zekert-III, 1977:**

Zekert F. Prophylaxe von phlebothrombosen und lungenembolien mit aggregationshemmemn In: Zekert F, ed. *Thrombosen, Embolien und Aggregatonsheimsnerin derChirurgie*. Stuttgart: Schattauer, 1975:75-88.

### **Harjola DVT, 1982:**

Harjola P, Meurala H, Frick AMH. Prevention of deep venous theornboss and thrombo-embolism by dipyridamole and acetylsalicylic acid atter re.oastruvuve artenal surgery *JCardotzasc Surg* 1980U21:451-4.



**Weiss, 1977:**

Weiss V, Jekiel M, Ritschard J, Bouvier CA. Prevention of the thromboembolic disease postoperative by anti-thrombotic agents in orthopedic surgery. *Medicine and Hygiene (Geneve)* 1977;35:943-4.

**Canata, 2003:**

Canata GL, Chiey A. Prevention of venous thromboembolism after ACL reconstruction: a prospective, randomized study. (*International Society of Arthroscopy, Knee Surgery and Orthopaedic Sports Medicine*) 2003; Vol. Poster 71-2003.

**Scurr, 1981:**

Scurr JH, Robbe IJ, Ellis H, Goldsmith HS Simple mechanical method for decreasing the incidence of thromboembolism. *Am J Surg* 1981;141:582-5 [[7223954](#)]

**Wilson, 1992:**

Wilson NV, Das SK, Kakkar VV, Maurice HD, Smibert JG, Thomas EM, Nixon JE Thrombo-embolic prophylaxis in total knee replacement. Evaluation of the A-V Impulse System. *J Bone Joint Surg Br* 1992 Jan;74:50-2 [[1732265](#)]

**65279;Blackshear excluder, 1987:**

Blackshear WM Jr, Prescott C, LePain F, Benoit S, Dickstein R, Seifert KB Influence of sequential pneumatic compression on postoperative venous function. *J Vasc Surg* 1987;5:432-6 [[3509596](#)]

**Hull II, 1990:**

Hull RD, Raskob GE, Gent M, McLoughlin D, Julian D, Smith FC, Dale NI, Reed-Davis R, Lofthouse RN, Anderson C Effectiveness of intermittent pneumatic leg compression for preventing deep vein thrombosis after total hip replacement. *JAMA* 1990;263:2313-7 [[2182917](#)]

**Fisher, 1995:**

Fisher CG, Blachut PA, Salvian AJ, Meek RN, O'Brien PJ Effectiveness of pneumatic leg compression devices for the prevention of thromboembolic disease in orthopaedic trauma patients: a prospective, randomized study of compression alone versus no prophylaxis. *J Orthop Trauma* 1995;9:1-7 [[7714648](#)]

**Turpie II, 1979:**

Turpie AG, Delmore T, Hirsh J, Hull R, Genton E, Hiscoe C, Gent M Prevention of venous thrombosis by intermittent sequential calf compression in patients with intracranial disease. *Thromb Res* 1979;15:611-6 [[494166](#)]

**Knudson, 1994:**

Knudson MM, Lewis FR, Clinton A, Atkinson K, Megerman J Prevention of venous thromboembolism in trauma patients. *J Trauma* 1994;37:480-7 [[8083913](#)]

**Kosir, 1996:**

Kosir MA, Kozol RA, Perales A, McGee K, Beleski K, Lange P, Dahn M Is DVT prophylaxis overemphasized? A randomized prospective study. *J Surg Res* 1996;60:289-92 [[8598656](#)] [10.1006/jsre.1996.0045](#)

**KANT (7 days), 2008:**

Camporese G, Ntita K, Rossi F, Bernardi E, Verlato F, Salmistraro G, Cordova R, et al. Different thromboprophylaxis approaches in patients undergoing knee arthroscopy (KANT study): interim report of prospective randomized study. *Journal of Thrombosis Haemostasis*.

Camporese G, Bernardi E, Prandoni P, Noventa F, Verlato F, Simioni P, Ntita K, Salmistraro G, Frangos C, Rossi F, Cordova R, Franz F, Zucchetta P, Kontothanassis D, Andreozzi GM Low-molecular-weight heparin versus compression stockings for thromboprophylaxis after knee arthroscopy: a randomized trial. *Ann Intern Med* 2008;149:73-82 [[18626046](#)]

**Roth, 1995:**

Roth P. Prophylaxis of deep vein thrombosis in outpatients undergoing arthroscopic meniscus operation. *Orthopdische Praxis* 1995;5:3458.

**Kujath, 1993:**

Kujath P, Spannagel U, Habscheid W Incidence and prophylaxis of deep venous thrombosis in outpatients with injury of the lower limb. *Haemostasis* 1993;23 Suppl 1:20-6 [[8388353](#)]

**KANT (14 days), 2008:**

Camporese G, Bernardi E, Prandoni P, Noventa F, Verlato F, Simioni P, Ntita K, Salmistraro G, Frangos C, Rossi F, Cordova R, Franz F, Zucchetta P, Kontothanassis D, Andreozzi GM Low-molecular-weight heparin versus compression stockings for thromboprophylaxis after knee arthroscopy: a randomized trial. *Ann Intern Med* 2008;149:73-82 [[18626046](#)]

**Wirth, 2001:**

Wirth T, Schneider B, Misselwitz F, Lomb M, Tyl H, Egbring R, Griss P Prevention of venous thromboembolism after knee arthroscopy with low-molecular weight heparin (reviparin): Results of a randomized controlled trial. *Arthroscopy* 2001;17:393-9 [[11288011](#)]

**Jorgensen, 2002:**

Jrgensen PS, Warming T, Hansen K, Paltved C, Vibeke Berg H, Jensen R, Kirchhoff-Jensen R, Kjaer L, Kerbouche N, Leth-Espensen P, Narvestad E, Rasmussen SW, Sloth C, Trholm C, Wille-Jrgensen P Low molecular weight heparin (Innohep) as thromboprophylaxis in outpatients with a plaster cast: a venographic controlled study. *Thromb Res* 2002;105:477-80 [[12091045](#)]

**Smith (D), 1978:**

Smith RC, Elton RA, Orr JD, Hart AJ, Graham IF, Fuller GA, Rundle JS, Macpherson AI, Ruckley CV Dextran and intermittent pneumatic compression in prevention of postoperative deep vein thrombosis: multiunit trial. *Br Med J* 1978;1:952-4 [[638545](#)]

**APEX, 2016:**

Cohen AT, Harrington RA, Goldhaber SZ, Hull RD, Wiens BL, Gold A, Hernandez AF, Gibson CM Extended Thromboprophylaxis with Betrixaban in Acutely Ill Medical Patients. *N Engl J Med* 2016 May 27;: [[27232649](#)]

**FX140, Simonneau G, 2006:**

Simonneau G, Laporte S, Mismetti P, Derlon A, Samii K, Samama CM, Bergman JF A randomized study comparing the efficacy and safety of nadroparin 2850 IU (0.3 mL) vs. enoxaparin 4000 IU (40 mg) in the prevention of venous thromboembolism after colorectal surgery for cancer. *J Thromb Haemost* 2006;4:1693-700 [[16796710](#)]

Simonneau G, Laporte S, Mismetti P, Derlon A, Samii K, Samama CM, Bergman JF A randomized study comparing the efficacy and safety of nadroparin 2850 IU (0.3 mL) vs. enoxaparin 4000 IU (40 mg) in the prevention of venous thromboembolism after colorectal surgery for cancer. *J Thromb Haemost* 2006 Aug;4:1693-700 [[16796710](#)]

**SAVE-HIP1, 2012:**

Lassen MR, Fisher W, Mouret P, Agnelli G, George D, Kakkar A, Mismetti P, Turpie AG Semuloparin for prevention of venous thromboembolism after major orthopedic surgery: results from three randomized clinical trials, SAVE-HIP1, SAVE-HIP2 and SAVE-KNEE. *J Thromb Haemost* 2012;10:822-32 [[22429800](#)] [10.1111/j.1538-7836.2012.04701.x](#)

**SAVE-KNEE, 2012:**

Lassen MR, Fisher W, Mouret P, Agnelli G, George D, Kakkar A, Mismetti P, Turpie AG Semuloparin for prevention of venous thromboembolism after major orthopedic surgery: results from three randomized clinical trials, SAVE-HIP1, SAVE-HIP2 and SAVE-KNEE. *J Thromb Haemost* 2012 May;10:822-32 [[22429800](#)] [10.1111/j.1538-7836.2012.04701.x](#)

**SAVE-HIP 2, 2012:**

Lassen MR, Fisher W, Mouret P, Agnelli G, George D, Kakkar A, Mismetti P, Turpie AG Semuloparin for prevention of venous thromboembolism after major orthopedic surgery: results from three randomized clinical trials, SAVE-HIP1, SAVE-HIP2 and SAVE-KNEE. *J Thromb Haemost* 2012 May;10:822-32 [[22429800](#)] [10.1111/j.1538-7836.2012.04701.x](#)

**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](#)

**Elliott, 1999:**

Elliott CG, Dudney TM, Egger M, Orme JF, Clemmer TP, Horn SD, Weaver L, Handrahan D, Thomas F, Merrell S, Kitterman N, Yeates S Calf-thigh sequential pneumatic compression compared with plantar venous pneumatic compression to prevent deep-vein thrombosis after non-lower extremity trauma. *J Trauma* 1999;47:25-32 [[10421182](#)]

**Gelfer, 2006:**

Gelfer Y, Tavor H, Oron A, Peer A, Halperin N, Robinson D Deep vein thrombosis prevention in joint arthroplasties: continuous enhanced circulation therapy vs low molecular weight heparin. *J Arthroplasty* 2006 Feb;21:206-14 [[16520208](#)]

**Pasteyer, 1977:**

Flicoteaux H, Kher A, Jean N, Blery M, Judet T, Honnart F, et al. Comparison of low dose heparin and low dose herparin combined with aspirin in prevention of deep vein thrombosis after total hip replacement. *Pathol Biol (Paris)* 1977;25(suppl):55-8.

**Rocha, 1986:**

Alfaro MJ, Pramo JA, Rocha E Prophylaxis of thromboembolic disease and platelet-related changes following total hip replacement: a comparative study of aspirin and heparin-dihydroergotamine. *Thromb Haemost* 1986;56:53-6 [3535158]

**Morris-B , 1977:**

Morris GK, Mitchell JR Preventing venous thromboembolism in elderly patients with hip fractures: studies of low-dose heparin, dipyridamole, aspirin, and flurbiprofen. *Br Med J* 1977;1:535-7 [843794]

**Lyon-I, 1975:**

Dechavanne M, Ville D, Viala JJ, Kher A, Faivre J, Pousset MB, Dejour H Controlled trial of platelet anti-aggregating agents and subcutaneous heparin in prevention of postoperative deep vein thrombosis in high risk patients. *Haemostasis* 1975;4:94-100 [1205340]

**Morris-A , 1977:**

Morris GK, Mitchell JR Preventing venous thromboembolism in elderly patients with hip fractures: studies of low-dose heparin, dipyridamole, aspirin, and flurbiprofen. *Br Med J* 1977;1:535-7 [843794]

**Ho [43], :**

Ho YH, Seow-Choen F, Leong A, Eu KW, Nyam D, Teoh MK Randomized, controlled trial of low molecular weight heparin vs. no deep vein thrombosis prophylaxis for major colon and rectal surgery in Asian patients. *Dis Colon Rectum* 1999;42:196-202; discussion 202-3 [10211496]

**Warwick, 1995:**

Warwick D, Bannister GC, Glew D, Mitchelmore A, Thornton M, Peters TJ, Brookes S Perioperative low-molecular-weight heparin. Is it effective and safe. *J Bone Joint Surg Br* 1995 Sep;77:715-9 [7559695]

**Marassi [41], :**

Marassi A, Balzano G, Mari G, D'Angelo SV, Della Valle P, Di Carlo V, D'Angelo A Prevention of postoperative deep vein thrombosis in cancer patients. A randomized trial with low molecular weight heparin (CY 216). *Int Surg* 1993;78:166-70 [8394842]

**Yoo, 1997:**

Yoo MC, Kang CS, Kim YH, Kim SK A prospective randomized study on the use of nadroparin calcium in the prophylaxis of thromboembolism in Korean patients undergoing elective total hip replacement. *Int Orthop* 1997;21:399-402 [9498151]

**PROTECT (nadroparin), :**

ongoing trial NCT00881088

**Pinto, 1970:**

Pinto DJ Controlled trial of an anticoagulant (warfarin sodium) in the prevention of venous thrombosis following hip surgery. *Br J Surg* 1970;57:349-52 [5427880]

**Hume, 1973:**

Hume M, Kuriakose TX, Zuch L, Turner RH 125I fibrinogen and the prevention of venous thrombosis. *Arch Surg* 1973;107:803-6 [4744294]

**Morris, 1976:**

Morris GK, Mitchell JR Warfarin sodium in prevention of deep venous thrombosis and pulmonary embolism in patients with fractured neck of femur. *Lancet* 1976;2:869-72 [62111]

**Powers, 1989:**

Powers PJ, Gent M, Jay RM, Julian DH, Turpie AG, Levine M, Hirsh J A randomized trial of less intense postoperative warfarin or aspirin therapy in the prevention of venous thromboembolism after surgery for fractured hip. *Arch Intern Med* 1989;149:771-4 [2650646]

**Levine, 1996:**

Levine MN, Gent M, Hirsh J, Weitz J, Turpie AG, Powers P, Neemeh J, Willan A, Skingley P Ardeparin (low-molecular-weight heparin) vs graduated compression stockings for the prevention of venous thromboembolism. A randomized trial in patients undergoing knee surgery. *Arch Intern Med* 1996 Apr 22;156:851-6 [8774203]

**MRC, 1972:**

Effect of aspirin on postoperative venous thrombosis. Report of the Steering Committee of a trial sponsored by the Medical Research Council. *Lancet* 1972;2:441-5 [4115340]

**Loew DVT, 1974:**

Loew D, Wellmer HK, Baer U, Merguet H, Rumpf P, Petersen H, et al. Postoperative thromboembolie-prophylaxe mit acetylsalicylsäure. *Duch Med Wschr* 1974;99:565-72.

**Erfurt-A, 1979:**

Schreiber U, Hartung B. Postoperative thromboembolieprophylaxe bei patienten mit allgemein chirurgischen operationen Chirur 1979;104: 1214-20.

**Zekert V, 1980:**

Zekert F, Hofbauer F, Mhlbacher F [Prophylaxis of thromboembolism in abdominal surgery. Comparison of low dose heparin, acetylsalicylic acid and their combination (author's transl)] MMW Munch Med Wochenschr 1980;122:1495-8 [6780841]

**Vinazzer I, 1980:**

Vinazzer H, Loew D, Simma W, Brcke P Prophylaxis of postoperative thromboembolism by low dose heparin and by acetylsalicylic acid given simultaneously. A double blind study. Thromb Res 1980;17:177-84 [7376128]

**Vinazzer II, 1977:**

Loew D, Brcke P, Simma W, Vinazzer H, Dienstl E, Boehme K Acetylsalicylic acid, low dose heparin, and a combination of both substances in the prevention of postoperative thromboembolism. A double blind study. Thromb Res 1977;11:81-6 [329468]

**Zekert-I , 1974:**

Zekert F, Kohn P, Vormittag E, Poigenfrst J, Thien M [Prevention of thromboembolism using acetylsalicylic acid in the surgery of hip-joint proximal fractures] Monatsschr Unfallheilkd Versicher Versorg Verkehrsmed 1974;77:97-110 [4277091]

**Powers , 1976:**

Hansen EH, Jessing P, Lindewald H, Ostergaard P, Olesen T, Malver EI Hydroxychloroquine sulphate in prevention of deep venous thrombosis following fracture of the hip, pelvis, or thoracolumbar spine. J Bone Joint Surg Am 1976;58:1089-93 [1002750]

Powers PJ, Gent M, Jay RM, Julian DH, Turpie AG, Levine M, Hirsh J A randomized trial of less intense postoperative warfarin or aspirin therapy in the prevention of venous thromboembolism after surgery for fractured hip. Arch Intern Med 1989;149:771-4 [2650646]

**Erfurt-B , 1979:**

Hartung B, Schreiber U, Rdiger H [Study of the platelet aggregation inhibitor MICRISTIN as to its efficacy in the prevention of thromboembolism in the postoperative phase following surgical interventions] Folia Haematol Int Mag Klin Morphol Blutforsch 1979;106:810-27 [94873]

**PEP hip-fracture, 2000:**

Prevention of pulmonary embolism and deep vein thrombosis with low dose aspirin: Pulmonary Embolism Prevention (PEP) trial. Lancet 2000 Apr 15;355:1295-302 [10776741]

**PEP elective arthroplasty, 2000:**

Prevention of pulmonary embolism and deep vein thrombosis with low dose aspirin: Pulmonary Embolism Prevention (PEP) trial. Lancet 2000 Apr 15;355:1295-302 [10776741]

**Stockholm-I, 1975:**

Soreff J, Johnsson H, Diener L, Gransson L Acetylsalicylic acid in a trial to diminish thromboembolic complications after elective hip surgery. Acta Orthop Scand 1975;46:246-55 [1096521]

**Harris-I, 1977:**

Harris WH, Salzman EW, Athanasoulis CA, Waltman AC, DeSanctis RW Aspirin prophylaxis of venous thromboembolism after total hip replacement. N Engl J Med 1977;297:1246-9 [335247]

**McKenna-I, 1980:**

McKenna R, Galante J, Bachmann F, Wallace DL, Kaushal PS, Meredith P Prevention of venous thromboembolism after total knee replacement by high-dose aspirin or intermittent calf and thigh compression. Br Med J 1980;280:514-7 [6989432]

**Sautter, 1983:**

Sautter RD, Koch EL, Myers WO, Ray JR 3rd, Mazza JJ, Larson DE, Chen HM, Milbauer JP, Treuhaft PS, Plotka ED Aspirin-sulfinpyrazone in prophylaxis of deep venous thrombosis in total hip replacement. JAMA 1983;250:2649-54 [6355542]

**McBride, 1983:**

McBride JA, Turpie AG, Kraus V, Hiltz C. Failure of aspirin and dipyridamole to influence the incidence of leg scan detected venous thrombosis after elective hip surgery Thrombosis et Diathesis Haemorrhagica 1975;34:abstract 204.

**Encke-II , 1976:**

Encke A, Stock C, Dumke HO [Double-blind study for the prevention of postoperative thrombosis] Chirur 1976;47:670-3 [1001131]

**Hamburg, 1976:**

Boehringer Ingelheim DVT nach Hirntumoroperationen Boehringer Ingelheim, 1976. (Internal report.)

**Frankfurt, 1981:**

unpublished

Boehringer Ingelheim. Asasantin DVT nach myokardinfarkt Bracknell Berkshire: Boehringer Ingelheim, 1981. (Internal report.)

**D-Kaf (Selby), 2007:**

Geerts WH, Pineo GF, Heit JA, Bergqvist D, Lassen MR, Colwell CW, Ray JG Prevention of venous thromboembolism: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. Chest 2004;126:338S-400S [[15383478](#)] [10.1378/chest.126.3\\_suppl.338S](#)

**Leizorovicz, 2004:**

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](#)]

**Jorgensen, 1989:**

**Torholm, 1991:**

Torholm C, Broeng L, Jorgensen PS, Bjerregaard P, Josephsen L, Jorgensen PK, Hagen K, Knudsen JB Thromboprophylaxis by low-molecular-weight heparin in elective hip surgery. A placebo controlled study. J Bone Joint Surg Br 1991 May;73:434-8 [[1670445](#)]

**Ockelford , 1989:**

Ockelford PA, Patterson J, Johns AS A double-blind randomized placebo controlled trial of thromboprophylaxis in major elective general surgery using once daily injections of a low molecular weight heparin fragment (Fragmin). Thromb Haemost 1989;62:1046-9 [[2559484](#)]

**Lapidus, 2007:**

Lapidus LJ, Rosfors S, Ponzer S, Levander C, Elvin A, Lrfars G, de Bri E Prolonged thromboprophylaxis with dalteparin after surgical treatment of achilles tendon rupture: a randomized, placebo-controlled study. J Orthop Trauma 2007;21:52-7 [[17211270](#)] [10.1097/01.bot.0000250741.65003.14](#)

**Lapidus, 2007:**

Lapidus LJ, Ponzer S, Elvin A, Levander C, Lrfars G, Rosfors S, de Bri E Prolonged thromboprophylaxis with Dalteparin during immobilization after ankle fracture surgery: a randomized placebo-controlled, double-blind study. Acta Orthop 2007;78:528-35 [[17966008](#)] [10.1080/17453670710014185](#)

## 13 diabetes type 2

Trial	Treatments	Patients	Trials design and methods
<b>alogliptin vs</b>			
<a href="#">Bosi , 2011</a> [NCT00432276] n=NA	-	-	
<a href="#">DeFronzo , 2008</a> [NCT00286455] n=NA	-	-	
<a href="#">Kaku , 2011</a> n=NA follow-up:	-	-	Japan
<a href="#">Pratley , 2009</a> [NCT00286468] n=NA follow-up:	-	-	

continued...

Trial	Treatments	Patients	Trials design and methods
Pratley , 2009 [NCT00286494] n=NA follow-up:	-	-	
Rosenstock , 2009 [NCT00286429] n=NA follow-up:	-	-	
Rosenstock , 2010 [NCT00395512] n=NA follow-up:	-	-	
Seino , 2011 [NCT01263509] n=NA follow-up:	-	-	
Seino , 2011 n=NA follow-up:	-	-	Japan
<b>dapagliflozin vs</b>			
Yang , 2015 [NCT01095666] n=NA follow-up:	-	-	China
<b>empagliflozin vs</b>			
Kadowaki , 2013 n=NA follow-up:	-	Japanese patients with type 2 diabetes	
Kadowaki , 2014 n=NA	-	-	
<b>glargine vs</b>			
Eliaschewitz n=231/250 follow-up: 24 weeks	-	-	
Fonseca n=52/48 follow-up: 28 weeks	-	-	
Massi n=293/285 follow-up: 52 weeks	-	-	
Pan n=220/223 follow-up: 24 weeks	-	-	

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>Philis-Tsimikas</b> n=334/164 follow-up: 20 weeks	-	-	
<b>Rosenstock</b> n=259/259 follow-up: 28 weeks	-	-	
<b>Wang</b> n=16/8 follow-up: 12 weeks	-	-	
<b>Yki-Yarvinen</b> n=214/208 follow-up: 52 weeks	-	-	
<b>Yki-Yarvinen</b> n=61/49 follow-up: 36 weeks	-	-	
<b>Yokoyama</b> n=31/31 follow-up: 26 weeks	-	-	
<b>linagliptin vs</b>			
<b>Forst , 2010</b> [NCT00309608] n=NA follow-up: 12 weeks	Linagliptin (1, 5, or 10 mg taken once daily) versus placebo (on top Metformin )	patients with type 2 diabetes mellitus who are not at goal with their HbA1c levels	double-blind France
<b>liraglutide other doses vs</b>			
<b>NN2211-1333</b> n=NA follow-up:	liraglutide versus placebo	obese subjects with type 2 diabetes	
<b>rosiglitazone vs</b>			
<b>AVM100264</b> [NCT00359112] n=294/302 follow-up: 52 wk	Rosiglitazone and metformin versus Metformin and sulfonylurea	Overweight patients with type 2 DM poorly controlled on Met	Parallel groups
<b>BRL 49653C/185</b> n=563/142 follow-up: 32 wk	Rosiglitazone with or without metformin versus Usual care with or without metformin	patients with type 2 diabetes	Parallel groups
<b>SB-712753/007</b> n=314/154 follow-up: 32 wk	Rosiglitazone with or without metformin versus Metformin	patients with type 2 diabetes without previous drug therapy	Parallel groups
<b>SB-712753/009</b> n=162/160 follow-up: 24 wk	Rosiglitazone, metformin, and insulin versus Insulin	patients with type 2 diabetes with insulin	Parallel groups
<b>saxagliptin vs</b>			

continued...

Trial	Treatments	Patients	Trials design and methods
Fonseca , 2012 [NCT00960076] n=NA follow-up:	-	-	
Forst , 2011 n=NA	-	-	
Gke , 2010 n=NA follow-up:	-	-	
Kawamori , 2012 [NCT00654381] n=NA follow-up:	-	-	
Nowicki , 2011 [NCT00614939] n=NA follow-up:	-	-	
Nowicki , 2011 [NCT00614939] n=NA follow-up:	-	-	
Scheen , 2010 n=NA	-	-	
Stenlf , 2010 n=NA	-	-	
Yang , 2011 [NCT00661362] n=NA follow-up:	-	-	
<b>sitagliptin vs</b>			
Stafford , 2011 [NCT00451113] n=NA follow-up:	-	older adults with type 2 diabetes mellitus	
<b>tesaglitazar vs</b>			
GALLANT 9 [NCT00242372] n=NA	-	-	
GALLANT 7 [NCT00251940] n=NA	-	-	

continued...



Trial	Treatments	Patients	Trials design and methods
<b>GALLANT 8</b> [NCT00251953] n=NA	-	-	
<b>GALLANT 6</b> [NCT00214565] n=NA	-	-	
<b>D6160C00028</b> [NCT00255541] n=NA	-	-	
<b>D6160C00026</b> [NCT00252772] n=NA	-	-	
<b>GALLANT 14</b> [NCT00261352] n=NA	-	-	
<b>D6160C00055</b> [NCT00252837] n=NA	-	-	
<b>D6160C00040</b> [NCT00229684] n=NA	-	-	
<b>vildagliptin vs</b> <b>NCT00101673</b> [NCT00101673] n=NA follow-up:	-	-	
<b>repaglinide vs ???</b> <b>YSRE0001</b> [NCT00336310] n=NA follow-up: 12 weeks	Repaglinide versus NA	-	double-blind Taiwan
<b>vildagliptin monotherapy vs acarbose</b> <b>Pan , 2008</b> [NCT00110240] n=441/220 follow-up: 24 weeks	vildagliptin (100 mg daily, given as 50 mg twice daily versus acarbose (up to 300 mg daily, given as three equally divided doses	drug-naive patients with Type 2 diabetes	double-blind
<b>AHA 2 diet vs AHA 1 diet</b>			

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
Liao , 2002 n=70 follow-up: 22 months	American Heart Association (AHA) step 2 diet (<30% of total calories as fat, <7% saturated fat, 55% carbohydrate, and <200 mg cholesterol daily) plus endurance exercise for 1 h three times a week versus AHA step 1 diet (30% of total calories as fat, 10% saturated fat, 50% carbohydrate, and <300 mg cholesterol) plus stretching exercise three times a week	Japanese American subjects with impaired glucose tolerance (WHO criteria 1998)	Parallel groups open USA
<b>lispro thrice daily vs basal insulin</b>			
Raz , 2009 n=NA follow-up:	three premeal doses of insulin lispro versus NPH twice daily or insulin glargine once daily	patients with type 2 diabetes after acute myocardial infarction	
<b>prandial plus basal vs basal insulin</b>			
Hirsch A VOIR (MA) n=NA follow-up:	insulin lispro protamine suspension plus insulin lispro versus basal insulin glargine	metformin-treated patients with type 2 diabetes	
<b>prandial premixed therapy vs basal/bolus therapy</b>			
Garber , 2006 n=NA follow-up:	prandial premixed therapy versus basal/bolus therapy	-	
<b>prandial premixed therapy tid vs basal/bolus therapy</b>			
Rosenstock , 2008 n=NA follow-up:	lispro mix 50/50: 50% insulin lispro protamine suspension and 50% lispro 3 times daily (prandial premixed therapy) versus glargine at bedtime plus mealtime lispro (basal/bolus therapy)	-	
<b>morning insulin glargine vs bedtime insulin glargine</b>			
Fritche n=463/232 follow-up: 24 weeks	morning insulin glargine versus bedtime insulin glargine	patients with type 2 diabetes previously treated with oral antidiabetic agents	open
<b>basal-bolus therapy vs biphasic insulin aspart 30</b>			
Liebl , 2009 n=NA follow-up:	analogue basal-bolus therapy (insulin detemir once daily and insulin aspart mealtimes) versus biphasic insulin aspart 30 twice daily	-	
<b>glibenclamide vs c (add on MET)</b>			

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>Hermann , 1991</b> n=NA follow-up: 6 months	metformin + glibenclamide versus metformin	patients with non-insulin-dependent diabetes mellitus	Parallel groups
<b>aspart + basal vs continuous infusion</b>			
<b>Raskin , 2003</b> n=NA follow-up:	multiple daily injection bolus insulin aspart and basal NPH insulin versus continuous subcutaneous insulin infusion	-	
<b>lispro +glargine vs continuous infusion</b>			
<b>Herman , 2005</b> n=NA follow-up:	multiple daily injection using insulin lispro and insulin glargine versus continuous subcutaneous insulin infusion using insulin lispro	-	
<b>candesartan vs control</b>			
<b>SCOPE (diabetic subgroup) , 2003</b> n=313/284 follow-up: 3.7 years	candesartan versus control	sub group of diabetic patients aged 70-89 years, with systolic blood pressure 160-179 mmHg, and/or diastolic blood pressure 90-99 mmHg, and a Mini Mental State Examination (MMSE) test score >or= 24	Parallel groups double-blind 15 countries
<b>captopril or atenolol vs control</b>			
<b>UKPDS 38 , 1998</b> n=758/390 follow-up: 8.4y (median)	tight control of blood pressure aiming at a BP <150/85 (with the use of captopril or atenolol as main treatment, other treatment were added if the control criteria were not met) versus less tight control aiming at a blood pressure of <180/105 (avoiding treatment with ACE inhibitors or beta-blockers)	hypertensive patients with type 2 diabetes	Parallel groups open UK
<b>insulin glargine vs control</b>			
<b>ORIGINE , 2012</b> [NCT00069784] n=6264/6273 follow-up: 6.2 years	insulin glargine (with a target fasting blood glucose level of 95 mg per deciliter versus standard care	with cardiovascular risk factors plus impaired fasting glucose, impaired glucose tolerance, or type 2 diabetes	
<b>jiangtang bushen recipe vs control</b>			
<b>Fan , 2004</b> n=51 follow-up: 4.1 y	jiangtang bushen recipe 2-3 times/week versus placebo	patients with impaired glucose tolerance (WHO 1999 criteria)	Parallel groups open China
<b>lifestyle modification vs control</b>			

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
DPS (Lindström) , 2003 n=522 follow-up: 3.2y	individualized counseling aimed at reducing weight and intake of total and saturated fat, and increasing intake of fiber and physical activity versus control	Patients overweight with impaired glucose tolerance (WHO 1985 criteria)	Parallel groups open Finnish
Fang , 2004 n=178 follow-up:	-	subject with impaired glucose tolerance	Parallel groups China
JDPP (Sakane) , 2005 n=240 follow-up:	-	patients with impaired glucose tolerance (WHO 1999 criteria)	Parallel groups Japan
Keen , 1982 n=241 follow-up:	-	subject with impaired glucose tolerance	Parallel groups
Kosaka , 2005 n=356/102 follow-up: 3.64 y	to maintain body mass index (BMI) of <24.0 kg/m <sup>2</sup> and of <22.0 kg/m <sup>2</sup> , respectively, by diet and exercise. In the intervention group, detailed instructions on lifestyle were repeated every 3-4 months versus control	men with impaired glucose tolerance (WHO criteria 1980)	Parallel groups open Japan
Pan , 1997 n=530 follow-up: 6 y	three active treatment groups: diet only, exercise only, or diet plus exercise versus control	Patients with impaired glucosetolerance (WHO 1985 criteria)	Parallel groups open China
Tao , 2004 n=60 follow-up: 31 months	-	patients with impaired glucose tolerance (WHO 1999 criteria)	Parallel groups China
US-DDP (lifestyle) (Knowler) , 2002 n=1079/1082 follow-up: 2.8 years	lifestyle-modification intervention versus placebo	nondiabetic patients with elevated glucose and high risk for diabetes	Parallel groups open
<b>lifestyle modification + metformin vs control</b>			
IDDP (Ramachandran) , 2006 n=531 follow-up: 2.5 y	advice on lifestyle modification, metformin, or both versus given standard health care advice (control)	native Asian Indians with impaired glucose tolerance	Parallel groups open India

continued...

Trial	Treatments	Patients	Trials design and methods
Jarret , 1979 n=204 follow-up: 4.3 y	carbohydrate restriction with phenformin 50 mg daily versus carbohydrate restriction alone	men with impaired glucose toleranc	Parallel groups open
<b>rosiglitazone vs control</b>			
Wang , 2005 n=NA follow-up: 6 months	rosiglitazone 4 mg/d versus control	patients with diabetes and CAD who had undergone percutaneous coronary intervention	Parallel groups open

More details and results :

- antidiabetic drugs for diabetes type 2 in all types of patients at <http://www.trialresultscenter.org/go-Q81>
- anti hypertensive agents for diabetes type 2 in patients with hypertension at <http://www.trialresultscenter.org/go-Q83>
- cholesterol lowering intervention for diabetes type 2 in diabetic patients with or without hypercholesterolemia at <http://www.trialresultscenter.org/go-Q85>
- antiplatelets drug for diabetes type 2 in patients without cardiovascular disease at <http://www.trialresultscenter.org/go-Q221>
- antioxydants for diabetes type 2 in all type of patients at <http://www.trialresultscenter.org/go-Q231>
- screening for CAD for diabetes type 2 in all type of patients at <http://www.trialresultscenter.org/go-Q285>
- insulin sensitizers - glitazones for diabetes type 2 in all type of patients at <http://www.trialresultscenter.org/go-Q321>
- prevention for diabetes type 2 in all type of patients at <http://www.trialresultscenter.org/go-Q341>
- antiplatelets drug for diabetes type 2 in all type of patients at <http://www.trialresultscenter.org/go-Q362>
- insulin sensitizers - glitazones for diabetes type 2 in patients with cardiovascular disease at <http://www.trialresultscenter.org/go-Q376>
- insulin sensitizer for diabetes type 2 in all type of patients at <http://www.trialresultscenter.org/go-Q377>
- insulin sensitizer for diabetes type 2 in patients with cardiovascular disease at <http://www.trialresultscenter.org/go-Q378>
- insulin secretagogues peptides (incretins) for diabetes type 2 in all type of patients at <http://www.trialresultscenter.org/go-Q381>
- insulin secretagogues for diabetes type 2 in all type of patients at <http://www.trialresultscenter.org/go-Q409>
- anti hypertensive agents for diabetes type 2 in patients with or without hypertension at <http://www.trialresultscenter.org/go-Q414>
- prevention for diabetes type 2 in people with impaired glucose tolerance at <http://www.trialresultscenter.org/go-Q416>
- angiotensin-receptor blockers for diabetes type 2 in all type of patients at <http://www.trialresultscenter.org/go-Q427>
- angiotensin renin system blockade for diabetes type 2 in all type of patients at <http://www.trialresultscenter.org/go-Q438>
- intensive therapy for diabetes type 2 in all type of patients at <http://www.trialresultscenter.org/go-Q459>
- SGLT2 inhibitors for diabetes type 2 in all type of patients at <http://www.trialresultscenter.org/go-Q479>

## References

**Bosi , 2011:**

Bosi E, Ellis GC, Wilson CA, Fleck PR Alogliptin as a third oral antidiabetic drug in patients with type 2 diabetes and inadequate glycaemic control on metformin and pioglitazone: a 52-week, randomized, double-blind, active-controlled, parallel-group study. Diabetes Obes Metab 2011;13:1088-96 [21733058] 10.1111/j.1463-1326.2011.01463.x

**DeFronzo , 2008:**

DeFronzo RA, Fleck PR, Wilson CA, Mekki Q Efficacy and safety of the dipeptidyl peptidase-4 inhibitor alogliptin in patients with type 2 diabetes and inadequate glycemic control: a randomized, double-blind, placebo-controlled study. *Diabetes Care* 2008;31:2315-7 [[18809631](#)] [10.2337/dc08-1035](#)

**Kaku, 2011:**

Kaku K, Itayasu T, Hiroi S, Hirayama M, Seino Y Efficacy and safety of alogliptin added to pioglitazone in Japanese patients with type 2 diabetes: a randomized, double-blind, placebo-controlled trial with an open-label long-term extension study. *Diabetes Obes Metab* 2011;13:1028-35 [[21682833](#)] [10.1111/j.1463-1326.2011.01460.x](#)

**Pratley, 2009:**

Pratley RE, Kipnes MS, Fleck PR, Wilson C, Mekki Q Efficacy and safety of the dipeptidyl peptidase-4 inhibitor alogliptin in patients with type 2 diabetes inadequately controlled by glyburide monotherapy. *Diabetes Obes Metab* 2009;11:167-76 [[19125778](#)] [10.1111/j.1463-1326.2008.01016.x](#)

**Pratley, 2009:**

Pratley RE, Reusch JE, Fleck PR, Wilson CA, Mekki Q Efficacy and safety of the dipeptidyl peptidase-4 inhibitor alogliptin added to pioglitazone in patients with type 2 diabetes: a randomized, double-blind, placebo-controlled study. *Curr Med Res Opin* 2009;25:2361-71 [[19650752](#)] [10.1185/03007990903156111](#)

**Rosenstock, 2009:**

Rosenstock J, Rendell MS, Gross JL, Fleck PR, Wilson CA, Mekki Q Alogliptin added to insulin therapy in patients with type 2 diabetes reduces HbA(1C) without causing weight gain or increased hypoglycaemia. *Diabetes Obes Metab* 2009;11:1145-52 [[19758359](#)] [10.1111/j.1463-1326.2009.01124.x](#)

**Rosenstock, 2010:**

Rosenstock J, Inzucchi SE, Seufert J, Fleck PR, Wilson CA, Mekki Q Initial combination therapy with alogliptin and pioglitazone in drug-naïve patients with type 2 diabetes. *Diabetes Care* 2010;33:2406-8 [[20724648](#)] [10.2337/dc10-0159](#)

**Seino, 2011:**

Seino Y, Fujita T, Hiroi S, Hirayama M, Kaku K Alogliptin plus voglibose in Japanese patients with type 2 diabetes: a randomized, double-blind, placebo-controlled trial with an open-label, long-term extension. *Curr Med Res Opin* 2011;27 Suppl 3:21-9 [[22106975](#)] [10.1185/03007995.2011.614936](#)

**Seino, 2011:**

Seino Y, Fujita T, Hiroi S, Hirayama M, Kaku K Efficacy and safety of alogliptin in Japanese patients with type 2 diabetes mellitus: a randomized, double-blind, dose-ranging comparison with placebo, followed by a long-term extension study. *Curr Med Res Opin* 2011;27:1781-92 [[21806314](#)] [10.1185/03007995.2011.599371](#)

**Yang, 2015:**

Yang W, Han P, Min KW, Wang B, Mansfield T, T'Joan C, Iqbal N, Johnsson E, Ptaszynska A Efficacy and safety of dapagliflozin in Asian patients with type 2 diabetes after metformin failure: A randomized controlled trial. *J Diabetes* 2015;: [[26589253](#)]

**Kadowaki, 2013:**

Kadowaki T, Haneda M, Inagaki N et al. Empagliflozin monotherapy for 12 weeks improves glycemic control in Japanese patients with type 2 diabetes (T2DM) *Diabetes* 2013; 62: A297298.

**Kadowaki , 2014:**

Kadowaki T, Haneda M, Inagaki N, Terauchi Y, Taniguchi A, Koiwai K, Rattunde H, Woerle HJ, Broedl UC Empagliflozin monotherapy in Japanese patients with type 2 diabetes mellitus: a randomized, 12-week, double-blind, placebo-controlled, phase II trial. *Adv Ther* 2014;31:621-38 [[24958326](#)]

**Eliaschewitz , :**

Eliaschewitz FG, Calvo C, Valbuena H, Ruiz M, Aschner P, Villena J, Ramirez LA, Jimenez J Therapy in type 2 diabetes: insulin glargine vs. NPH insulin both in combination with glimepiride. *Arch Med Res* 2006;37:495-501 [[16715577](#)]

**Fonseca , :**

Fonseca V, Bell DS, Berger S, Thomson S, Mecca TE A comparison of bedtime insulin glargine with bedtime neutral protamine hagedorn insulin in patients with type 2 diabetes: subgroup analysis of patients taking once-daily insulin in a multicenter, randomized, parallel group study. *Am J Med Sci* 2004;328:274-80 [[15545844](#)]

**Massi , :**

Massi Benedetti M, Humburg E, Dressler A, Ziemer M A one-year, randomised, multicentre trial comparing insulin glargine with NPH insulin in combination with oral agents in patients with type 2 diabetes. *Horm Metab Res* 2003;35:189-96 [[12734781](#)] [10.1055/s-2003-39080](#)

**Pan , :**

Pan CY, Sinnassamy P, Chung KD, Kim KW Insulin glargine versus NPH insulin therapy in Asian Type 2 diabetes patients. *Diabetes Res Clin Pract* 2007;76:111-8 [[17011662](#)] [10.1016/j.diabres.2006.08.012](#)

**Philis-Tsimikas , :**

Philis-Tsimikas A, Charpentier G, Clauson P, Ravn GM, Roberts VL, Thorsteinsson B Comparison of once-daily insulin detemir with NPH insulin added to a regimen of oral antidiabetic drugs in poorly controlled type 2 diabetes. *Clin Ther* 2006;28:1569-81 [[17157113](#)] [10.1016/j.clinthera.2006.10.020](#)

**Rosenstock , :**

Rosenstock J, Davies M, Home PD, Larsen J, Koenen C, Schernthaner G A randomised, 52-week, treat-to-target trial comparing insulin detemir with insulin glargine when administered as add-on to glucose-lowering drugs in insulin-naive people with type 2 diabetes. *Diabetologia* 2008;51:408-16 [[18204830](#)] [10.1007/s00125-007-0911-x](#)

**Wang , :**

Wang XL, Lu JM, Pan CY, Mu YM, Dou JT, Ba JM, Wang X Evaluation of the superiority of insulin glargine as basal insulin replacement by continuous glucose monitoring system. *Diabetes Res Clin Pract* 2007;76:30-6 [[16979255](#)] [10.1016/j.diabres.2006.08.005](#)

**Yki-Yarvinen , :**

Yki-Jrvinen H, Juurinen L, Alvarsson M, Bystedt T, Caldwell I, Davies M, Lahdenper S, Nijpels G, Vhtalo M Initiate Insulin by Aggressive Titration and Education (INITIATE): a randomized study to compare initiation of insulin combination therapy in type 2 diabetic patients individually and in groups. *Diabetes Care* 2007;30:1364-9 [[17384341](#)] [10.2337/dc06-1357](#)

**Yki-Yarvinen , :**

Yki-Jrvinen H, Dressler A, Ziemer M Less nocturnal hypoglycemia and better post-dinner glucose control with bedtime insulin glargine compared with bedtime NPH insulin during insulin combination therapy in type 2 diabetes. HOE 901/3002 Study Group. *Diabetes Care* 2000;23:1130-6 [[10937510](#)]

**Yokoyama , :**

Yokoyama H, Tada J, Kamikawa F, Kanno S, Yokota Y, Kuramitsu M Efficacy of conversion from bedtime NPH insulin to morning insulin glargine in type 2 diabetic patients on basal-prandial insulin therapy. *Diabetes Res Clin Pract* 2006;73:35-40 [[16513202](#)] [10.1016/j.diabres.2005.12.009](#)

**Forst, 2010:**

Forst T, Uhlig-Laske B, Ring A, Graefe-Mody U, Friedrich C, Herbach K, Woerle HJ, Dugi KA Linagliptin (BI 1356), a potent and selective DPP-4 inhibitor, is safe and efficacious in combination with metformin in patients with inadequately controlled Type 2 diabetes. *Diabet Med* 2010;27:1409-19 [[21059094](#)] [10.1111/j.1464-5491.2010.03131.x](#)

**NN2211-1333, :**

Harder H, Nielsen L, Tu DT, Astrup A The effect of liraglutide, a long-acting glucagon-like peptide 1 derivative, on glycemic control, body composition, and 24-h energy expenditure in patients with type 2 diabetes. *Diabetes Care* 2004;27:1915-21 [[15277417](#)]

**AVM100264 , :****BRL 49653C/185 , :****SB-712753/007 , :****SB-712753/009 , :****Fonseca, 2012:**

Fonseca V, Zhu T, Karyekar C, Hirshberg B Adding saxagliptin to extended-release metformin vs. uptitrating metformin dosage. *Diabetes Obes Metab* 2012;14:365-71 [[22192246](#)] [10.1111/j.1463-1326.2011.01553.x](#)

**Forst, 2011:****Gke, 2010:**

Gke B, Gallwitz B, Eriksson J, Hellqvist A, Gause-Nilsson I Saxagliptin is non-inferior to glipizide in patients with type 2 diabetes mellitus inadequately controlled on metformin alone: a 52-week randomised controlled trial. *Int J Clin Pract* 2010;64:1619-31 [[20846286](#)] [10.1111/j.1742-1241.2010.02510.x](#)

**Kawamori, 2012:**

Kawamori R, Inagaki N, Araki E, Watada H, Hayashi N, Horie Y, Sarashina A, Gong Y, von Eynatten M, Woerle HJ, Dugi KA Linagliptin monotherapy provides superior glycaemic control versus placebo or voglibose with comparable safety in Japanese patients with type 2 diabetes: a randomized, placebo and active comparator-controlled, double-blind study. *Diabetes Obes Metab* 2012;14:348-57 [[22145698](#)] [10.1111/j.1463-1326.2011.01545.x](#)

Horie Y, Hayashi N, Dugi K, Takeuchi M Design, statistical analysis and sample size calculation of a phase IIb/III study of linagliptin versus voglibose and placebo. *Trials* 2009;10:82 [[19732457](#)] [10.1186/1745-6215-10-82](#)

**Nowicki, 2011:**

Nowicki M, Rychlik I, Haller H, Warren M, Suchower L, Gause-Nilsson I, Shtzer KM Long-term treatment with the dipeptidyl peptidase-4 inhibitor saxagliptin in patients with type 2 diabetes mellitus and renal impairment: a randomised controlled 52-week efficacy and safety study. *Int J Clin Pract* 2011;65:1230-9 [[21977965](#)] [10.1111/j.1742-1241.2011.02812.x](#)

**Nowicki, 2011:**

Nowicki M, Rychlik I, Haller H, Warren ML, Suchower L, Gause-Nilsson I Saxagliptin improves glycaemic control and is well tolerated in patients with type 2 diabetes mellitus and renal impairment. *Diabetes Obes Metab* 2011;13:523-32 [[21332627](#)] [10.1111/j.1463-1326.2011.01382.x](#)

**Scheen , 2010:**

Scheen AJ, Charpentier G, Ostgren CJ, Hellqvist A, Gause-Nilsson I Efficacy and safety of saxagliptin in combination with metformin compared with sitagliptin in combination with metformin in adult patients with type 2 diabetes mellitus. *Diabetes Metab Res Rev* 2010;26:540-9 [[20824678](#)] [10.1002/dmrr.1114](#)

**Stenlf , 2010:**

Stenlf K, Raz I, Neutel J, Ravichandran S, Berglind N, Chen R Saxagliptin and metformin XR combination therapy provides glycaemic control over 24 hours in patients with T2DM inadequately controlled with metformin. *Curr Med Res Opin* 2010;26:2355-63 [[20804445](#)] [10.1185/03007995.2010.511090](#)

**Yang, 2011:**

Yang W, Pan CY, Tou C, Zhao J, Gause-Nilsson I Efficacy and safety of saxagliptin added to metformin in Asian people with type 2 diabetes mellitus: a randomized controlled trial. *Diabetes Res Clin Pract* 2011;94:217-24 [[21871686](#)] [10.1016/j.diabres.2011.07.035](#)

**Stafford , 2011:**

Stafford S, Elahi D, Meneilly GS Effect of the dipeptidyl peptidase-4 inhibitor sitagliptin in older adults with type 2 diabetes mellitus. *J Am Geriatr Soc* 2011;59:1148-9 [[21668924](#)] [10.1111/j.1532-5415.2011.03438.x](#)

**GALLANT 9, :**

**GALLANT 7, :**

**GALLANT 8, :**

**GALLANT 6, :**

**D6160C00028, :**

**D6160C00026, :**

**GALLANT 14, :**

**D6160C00055, :**

**D6160C00040, :**

**NCT00101673, :**

Pratley RE, Schweizer A, Rosenstock J, Foley JE, Banerji MA, Pi-Sunyer FX, Mills D, Dejager S Robust improvements in fasting and prandial measures of beta-cell function with vildagliptin in drug-naïve patients: analysis of pooled vildagliptin monotherapy database. *Diabetes Obes Metab* 2008;10:931-8 [[18093207](#)] [10.1111/j.1463-1326.2007.00835.x](#)

**YSRE0001, 0:**

**Pan, 2008:**

Pan C, Yang W, Barona JP, Wang Y, Niggli M, Mohideen P, Wang Y, Foley JE Comparison of vildagliptin and acarbose monotherapy in patients with Type 2 diabetes: a 24-week, double-blind, randomized trial. *Diabet Med* 2008;25:435-41 [[18341596](#)] [10.1111/j.1464-5491.2008.02391.x](#)

**Liao, 2002:**

Liao D, Asberry PJ, Shofer JB, Callahan H, Matthys C, Boyko EJ, Leonetti D, Kahn SE, Austin M, Newell L, Schwartz RS, Fujimoto WY Improvement of BMI, body composition, and body fat distribution with lifestyle modification in Japanese Americans with impaired glucose tolerance. *Diabetes Care* 2002;25:1504-10 [[12196418](#)]

**Raz, 2009:**

Raz I, Wilson PW, Strojek K, Kowalska I, Bozikov V, Gitt AK, Jermendy G, Campaigne BN, Kerr L, Milicevic Z, Jacober SJ, Effects of prandial versus fasting glycemia on cardiovascular outcomes in type 2 diabetes: the HEART2D trial. *Diabetes Care* 2009;32:381-6. [[19246588](#)] [10.2337/dc08-1671](#)

**Hirsch A VOIR (MA), 0:**

Hirsch IB, Yuan H, Campaigne BN, Tan MH, Impact of prandial plus basal vs basal insulin on glycemic variability in type 2 diabetic patients. *Endocr Pract* ;15:343-8. [[19454394](#)] [10.4158/EP08308.ORR](#)

**Garber, 2006:**



Rosenstock J, Ahmann AJ, Colon G, Scism-Bacon J, Jiang H, Martin S Advancing insulin therapy in type 2 diabetes previously treated with glargine plus oral agents: prandial premixed (insulin lispro protamine suspension/lispro) versus basal/bolus (glargine/lispro) therapy. *Diabetes Care* 2008;31:20-5 [[17934150](#)] [10.2337/dc07-1122](#)

**Rosenstock, 2008:**

Rosenstock J, Ahmann AJ, Colon G, Scism-Bacon J, Jiang H, Martin S Advancing insulin therapy in type 2 diabetes previously treated with glargine plus oral agents: prandial premixed (insulin lispro protamine suspension/lispro) versus basal/bolus (glargine/lispro) therapy. *Diabetes Care* 2008;31:20-5 [[17934150](#)] [10.2337/dc07-1122](#)

**Fritche , :**

Fritsche A, Schweitzer MA, Hring HU Glimepiride combined with morning insulin glargine, bedtime neutral protamine hagedorn insulin, or bedtime insulin glargine in patients with type 2 diabetes. A randomized, controlled trial. *Ann Intern Med* 2003;138:952-9 [[12809451](#)]

**Liebl, 2009:**

Liebl A, Prager R, Binz K, Kaiser M, Bergenstal R, Gallwitz B, , Comparison of insulin analogue regimens in people with type 2 diabetes mellitus in the PREFER Study: a randomized controlled trial. *Diabetes Obes Metab* 2009;11:45-52. [[18643839](#)] [10.1111/j.1463-1326.2008.00915.x](#)

**Hermann, 1991:**

Hermann LS, Bitzn PO, Kjellstrm T, Lindgrde F, Scherstn B Comparative efficacy of metformin and glibenclamide in patients with non-insulin-dependent diabetes mellitus. *Diabete Metab* 1991;17:201-8 [[1936477](#)]

**Raskin, 2003:**

Raskin P, Bode BW, Marks JB, Hirsch IB, Weinstein RL, McGill JB, Peterson GE, Mudaliar SR, Reinhardt RR Continuous subcutaneous insulin infusion and multiple daily injection therapy are equally effective in type 2 diabetes: a randomized, parallel-group, 24-week study. *Diabetes Care* 2003;26:2598-603 [[12941725](#)]

**Herman, 2005:**

Herman WH, Ilag LL, Johnson SL, Martin CL, Sinding J, Al Harthi A, Plunkett CD, LaPorte FB, Burke R, Brown MB, Halter JB, Raskin P A clinical trial of continuous subcutaneous insulin infusion versus multiple daily injections in older adults with type 2 diabetes. *Diabetes Care* 2005;28:1568-73 [[15983302](#)]

**SCOPE (diabetic subgroup), 2003:**

Lithell H, Hansson L, Skoog I, Elmfeldt D, Hofman A, Olofsson B, Trenkwalder P, Zanchetti A The Study on Cognition and Prognosis in the Elderly (SCOPE): principal results of a randomized double-blind intervention trial. *J Hypertens* 2003;21:875-86 [[12714861](#)] [10.1097/01.hjh.0000059028.82022.89](#)

Trenkwalder P, Elmfeldt D, Hofman A, Lithell H, Olofsson B, Papademetriou V, Skoog I, Zanchetti A The Study on COgnition and Prognosis in the Elderly (SCOPE) - major CV events and stroke in subgroups of patients. *Blood Press* 2005;14:31-7 [[15823945](#)] [10.1080/08037050510008823](#)

**UKPDS 38, 1998:**

Efficacy of atenolol and captopril in reducing risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 39. UK Prospective Diabetes Study Group. *BMJ* 1998;317:713-20 [[9732338](#)]

Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38. UK Prospective Diabetes Study Group. *BMJ* 1998;317:703-13 [[9732337](#)]

**ORIGINE, 2012:**

Gerstein HC, Bosch J, Dagenais GR, Daz R, Jung H, Maggioni AP, Pogue J, Probstfield J, Ramachandran A, Riddle MC, Rydn LE, Yusuf S Basal insulin and cardiovascular and other outcomes in dysglycemia. *N Engl J Med* 2012;367:319-28 [[22686416](#)]

**Fan, 2004:**

Fan GJ, Luo GB, Qin ML [Effect of jiangtang bushen recipe in intervention treatment of patients with impaired glucose tolerance] *Zhongguo Zhong Xi Yi Jie He Za Zhi* 2004;24:317-20 [[15143717](#)]

**DPS (Lindstrm), 2003:**

Lindstrm J, Eriksson JG, Valle TT, Aunola S, Cepaitis Z, Hakumki M, Hmlinen H, Ilanne-Parikka P, Keinen-Kiukaanniemi S, Laakso M, Louheranta A, Mannelin M, Martikkala V, Moltchanov V, Rastas M, Salminen V, Sundvall J, Uusitupa M, Tuomilehto J Prevention of diabetes mellitus in subjects with impaired glucose tolerance in the Finnish Diabetes Prevention Study: results from a randomized clinical trial. *J Am Soc Nephrol* 2003;14:S108-13 [[12819313](#)]

**Fang, 2004:**

WHO Expert Committee on Diabetes Mellitus: second report. *World Health Organ Tech Rep Ser* 1980;646:1-80 [[6771926](#)]

Fang YS, Li TY, Chen SY *Zhongguo Linchuang Kangfu* 2004;8:6562-3g

**JDPP (Sakane), 2005:**

Sakane N [Japan Diabetes Prevention Program] *Nippon Rinsho* 2005;63 Suppl 2:488-92 [[15779427](#)]

**Keen, 1982:**

Keen H, Jarrett RJ, Ward JD, Fuller JH Borderline diabetics and their response to tolbutamide. *Adv Metab Disord* 1973;2:Suppl 2:521-31 [[4720382](#)]

**Kosaka, 2005:**

Kosaka K, Noda M, Kuzuya T Prevention of type 2 diabetes by lifestyle intervention: a Japanese trial in IGT males. *Diabetes Res Clin Pract* 2005;67:152-62 [[15649575](#)] [10.1016/j.diabres.2004.06.010](#)

**Pan, 1997:**

Pan XR, Li GW, Hu YH, Wang JX, Yang WY, An ZX, Hu ZX, Lin J, Xiao JZ, Cao HB, Liu PA, Jiang XG, Jiang YY, Wang JP, Zheng H, Zhang H, Bennett PH, Howard BV Effects of diet and exercise in preventing NIDDM in people with impaired glucose tolerance. The Da Qing IGT and Diabetes Study. *Diabetes Care* 1997;20:537-44 [[9096977](#)]

**Tao, 2004:**

Tao LL, Deng YB, Fan XB, Bao QDm *Zhongguo Linchuang Kangfu* 2004;8:2912-3g

**US-DDP (lifestyle) (Knowler), 2002:**

Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, Walker EA, Nathan DM *N Engl J Med* 2002;346:393-403 [[11832527](#)]

**IDDP (Ramachandran), 2006:**

Ramachandran A, Snehalatha C, Mary S, Mukesh B, Bhaskar AD, Vijay V The Indian Diabetes Prevention Programme shows that lifestyle modification and metformin prevent type 2 diabetes in Asian Indian subjects with impaired glucose tolerance (IDPP-1). *Diabetologia* 2006;49:289-97 [[16391903](#)] [10.1007/s00125-005-0097-z](#)

**Jarret, 1979:**

Jarrett RJ, Keen H, Fuller JH, McCartney M Worsening to diabetes in men with impaired glucose tolerance ("borderline diabetes"). *Diabetologia* 1979;16:25-30 [[761734](#)]

**Wang, 2005:**

Wang G, Wei J, Guan Y, Jin N, Mao J, Wang X, Peroxisome proliferator-activated receptor-gamma agonist rosiglitazone reduces clinical inflammatory responses in type 2 diabetes with coronary artery disease after coronary angioplasty. *Metabolism* 2005;54:590-7. [[15877288](#)] [10.1016/j.metabol.2004.11.017](#)

## 14 venous thrombosis

Trial	Treatments	Patients	Trials design and methods
<b>dabigatran vs warfarin</b>			
<a href="#">RE-MEDY , 2011</a> [NCT00329238] n=1430/1426 follow-up: 6 to 36 months	dabigatran 150 mg twice daily for an additional period of 6 to 36 months versus warfarin (to maintain an international normalized ratio of 2.0 to 3.0) for an additional period of 6 to 36 months	Secondary prevention of VTE in patients with VTE who had initially received 3 to 12 months of anticoagulant therapy	Parallel groups double-blind
<a href="#">REMEDY , 2013</a> n=1430/1426 follow-up:	-	-	
<b>Enoxaparin vs acenocoumarol</b>			
<a href="#">Veiga , 2000</a> n=50/50 follow-up: 6-9 mo	UFH, APTT 1.52.0d followed by Enoxaparin 4,000 IU qd versus UFH, APTT 1.52.0d followed by Acenocoumarol target INR 2-3	patients with objective diagnosis of DVT by Venography	open

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>Nadroparin vs acenocoumarol</b>			
<b>Lopez-Beret , 2001</b> n=81/77 follow-up: 6-9 mo	LMWH, 1,025 IU/10 kg bid followed by Nadroparin 1,025 IU/10 kg bid versus LMWH, 1,025 IU/10 kg bid followed by Acenocoumarol target INR 2-3	patients with objective diagnosis of DVT by compression ultrasonography	open
<b>Lopaciuk , 1999</b> n=101/101 follow-up: 9 mo	LMWH, 85 UI/kg bid followed by Nadroparin 85 IU/kg qd versus LMWH, 85 UI/kg bid followed by Acenocoumarol target INR 2-3	patients with objective diagnosis of DVT by Venography	open
<b>Tinzaparin vs acenocoumarol</b>			
<b>Romera , 2009</b> n=119/122 follow-up: 12 months	tinzaparin SC 175 IU anti-Xa per kg once daily for 6 months versus acenocoumarol for target INR 2-3 for 6 months after initial LMWH (until INR 2-3)	patients with symptomatic proximal DVT of the lowerlimbs confirmed by compression duplex ultrasound scan	Parallel groups open Spain
<b>rivaroxaban 10mg vs aspirin</b>			
<b>EINSTEIN CHOICE (10mg) , 2017</b> [NCT02064439] n=1127/1131 follow-up:	Rivaroxaban 10 mg once daily for 12 months versus ASA (Acetylsalicylic Acid) 100 mg once daily for 12 months	Patients with confirmed symptomatic DVT (Deep Vein Thrombosis) or PE (Pulmonary embolism) who completed 6 or 12 months of treatment of anticoagulation	
<b>VKA vs control</b>			
<b>AUREC FVII , 2009</b> n=17/17 follow-up: 37 months mean	continue VKA for additional 24 months versus discontinuation	patients with first spontaneous VTE and FVIII levels >230 IU/dl after 6 months of VKA	
<b>DACUS (Siragusa) , 2008</b> [NCT00438230] n=88/92 follow-up:	anticoagulants for 9 additional months versus no treatment	with a first episode of deep vein thrombosis, treated with OAT for 3 months and with Residual vein thrombosis	
<b>DURAC II , 1997</b> n=116/111 follow-up: 4 years	anticoagulant therapy continued indefinitely versus six months of oral anticoagulant therapy	patients who had had a second episode of venous thromboembolism	
<b>PROLONG (Palarati) , 2006</b> [NCT00264277] n=105/122 follow-up: 1.4 years	resume treatment versus discontinue treatment	patients with a first unprovoked proximal deep-vein thrombosis or pulmonary embolism who had received a vitamin K antagonist for at least 3 months and with abnormal D-dimer testing 1 month after the discontinuation of anticoagulation	

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>WODIT DVT , 2001</b> n=134/133 follow-up: at least two years	continuation for nine additional months versus discontinuation	Patients with a first episode of idiopathic proximal deep venous thrombosis who had completed three months of oral anticoagulant therapy	
<b>WODIT PE , 2003</b> n=165/161 follow-up:	-	patients after a first episode of pulmonary embolism who had had 3 months of oral anticoagulant therapy without experiencing recurrence or bleeding	
<b>DDOAT2006 ongoing</b> [NCT00895505] n=300 follow-up: 24 months	Extension of OAT versus discontinuation	-	
<b>warfarin vs control</b>			
<b>Vitotec , 2009</b> n=27/25 follow-up:	continuation of warfarin for another 6 months versus discontinuation of warfarin	patients with idiopathic DVT After 6 months of standard therapy (heparin/LMWH, warfarin with target INR 2-3) and persistent echogenic masses of over 20% of venous diameter	
<b>Enoxaparin vs coumarin</b>			
<b>Gonzalez-Fajardo , 2008</b> n=85/80 follow-up: 1y, 5y	long-term anticoagulant treatment with enoxaparin during at least 3 months versus long-term anticoagulant treatment with coumarin during at least 3 months	patients with symptomatic, unilateral, first-episode DVT	Parallel groups open, blind assessment Spain
<b>tinzaparin vs dalteparin</b>			
<b>Wells (subgroup) , 2005</b> n=NA follow-up: 3 months	Tinzaparin 175 IU/kg SQ daily (warfarin started simultaneously and continued for 90 days) versus dalteparin 200 IU/kg daily for at least 5 days ((warfarin started simultaneously and continued for 90 days)	study subgroup of patients with cancer treated for upper or lower extremity DVT or PE in the outpatient setting	Parallel groups outcome assessment blinded
<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>			

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</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>aspirin vs discontinuation</b>			
<b>WARFASA , 2012</b> [NCT00222677] n=205/197 follow-up: 24.6 mo (median)	aspirin, 100 mg daily for 2 years versus placebo	patients with first-ever unprovoked venous thromboembolism who had completed 6 to 18 months of oral anticoagulant treatment	Parallel groups double-blind
<b>ASPIRE , 2012</b> [ACTRN12605000004662] n=411/411 follow-up: 37.2 montsh (median)	-	patients who had completed initial anticoagulant therapy after a first episode of unprovoked venous thromboembolism	
<b>dabigatran vs discontinuation</b>			
<b>RE-SONATE , 2011</b> [NCT00558259] n=681/662 follow-up:	dabigatran 150 mg twice daily for an additional period of 6 months versus placebo	Secondary prevention of VTE in patients with VTE who had completed 6-18 months of anticoagulant therapy	Parallel groups double-blind
<b>idraparinux vs discontinuation</b>			
<b>VanGogh extension , 2007</b> [NCT00071279] n=594/621 follow-up: 6 months	once-weekly injections of 2.5 mg of idraparinux for 6 months versus placebo	patients who had completed 6 months of prophylaxis with idraparinux or a vitamin K antagonist and in whom extended anticoagulation was warranted	Parallel groups
<b>rivaroxaban vs discontinuation</b>			
<b>EINSTEIN-extension , 2009</b> [NCT00439725] n=602/595 follow-up:	rivaroxaban 20 mg once-daily for an additional 6 or 12 months versus placebo	patients who had completed six to 12 months of anticoagulant treatment for an acute episode of VTE	Parallel groups double blind 28 countries
<b>warfarin vs discontinuation</b>			
<b>PROLONG (Palareti) , 2006</b> [NCT00264277] n=105/122 follow-up: 1.4 yeras	prolongation versus no anticoagulation	patients with an abnormal d-dimer level 1 month after the discontinuation of anticoagulation in patients with a first unprovoked proximal deep-vein thrombosis or pulmonary embolism who had received a vitamin K antagonist for at least 3 months	Parallel groups

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>PREVENT (Ridker) , 2003</b> n=255/253 follow-up: 2.1 years	extension with low-intensity warfarin (target INR, 1.5 to 2.0) versus placebo	Patients with idiopathic venous thromboembolism who had received full-dose anticoagulation therapy for a median of 6.5 months	Parallel groups
<b>Agnelli , 2003</b> n=NA follow-up: 33 months	continuation for 3 or 9 additional months of warfarin or other oral anticoagulant was adjusted to achieve a target INR between 2.0 and 3.0. versus discontinuation (after 3 months)	patients who had had 3 months of oral anticoagulant therapy without experiencing recurrence or bleeding after a first episode of pulmonary embolism	Parallel groups open Italy
<b>Agnelli , 2001</b> n=NA follow-up: 33 months	continuation for 9 additional months; warfarin or acenocoumarol adjusted to achieve a target INR between 2.0 and 3.0 versus discontinuation (after 3 months months)	Patients with a first episode of idiopathic proximal deep venous thrombosis who had completed three months of oral anticoagulant therapy	Parallel groups open Italy
<b>LAFIT (Kearon) , 1999</b> n=NA follow-up:	Continuation of the oral anticoagulant therapy up to 24 months, warfarin was adjusted to achieve a target INR between 2.0 and 3.0. versus discontinuation (after 3 months)	patients who had completed 3 months of anticoagulant therapy for a first episode of idiopathic venous thromboembolism	
<b>ELAET (Kearon) , 2004</b> n=NA follow-up: 11 months (after randomizatio)	continuation for 2 additional months of warfarin adjusted to achieve a target INR between 2.0 and 3.0. versus discontinuation (after 1 months)	-	Parallel groups double blind Canada, US
<b>Levine , 1995</b> n=NA follow-up: 11 months after randomization.	continuation for 2 months of warfarin adjusted INR value of 2.0 to 3.0 versus Discontinue oral anticoagulant therapy (after 1 months)	Patients with venographically confirmed acute proximal DVT who had received four weeks of warfarin after initial heparin and whose four week IPG was normal	Parallel groups double blind Canada, Italy
<b>DURAC (Schulman) , 1997</b> n=NA follow-up: Four years after randomization	indefinite warfarin or dicoumarol adjusted for a target INR between 2.0 and 2.85 versus 6 months warfarin or dicoumarol adjusted for a target INR between 2.0 and 2.85	-	Parallel groups open Sweden
<b>ximelagatran vs discontinuation</b>			
<b>THRIVE III , 2003</b> n=612/611 follow-up: 18 months	ximelagatran 24 mg twice daily for 18 months versus placebo for 18 months	patients with venous thromboembolism who had undergone six months of anticoagulant therapy	Parallel groups double blind 18 countries
<b>warfarin vs low intensity warfarin</b>			

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>ELATE , 2003</b> n=369/369 follow-up: 2.4 years mean	continue warfarin therapy with a target international normalized ratio (INR) of 2.0 to 3.0 versus target INR of 1.5 to 1.9 (low intensity)	patients who had completed three or more months of warfarin therapy for unprovoked venous thromboembolism	Parallel groups open-label
<b>arvin vs no fibrinolysis</b>			
<b>Kakkar (arvin) , 1969</b> n=NA follow-up:	streptokinase 500,000 U IV over 30 minutes, 900,000 U every 6 hours for 5 days versus heparin 10,000 U over 5 minutes, then 10,000 to 15,000 U every 6 hours for 5 days	patients with venographically confirmed DVT of leg of duration <4 days	Parallel groups single blind UK
<b>streptokinase vs no fibrinolysis</b>			
<b>Arneson , 1978</b> n=43 follow-up:	streptokinase 250,000 U loading IV, then 100,000 IU/hour IV 72-96 hours versus heparin 15,000 IU IV bolus, 30,000 IU infusion IV 72-90 hours	inpatients with venographically confirmed DVT extending proximally beyond the calf <5 days duration?	Parallel groups single blind Norway
<b>Common , 1976</b> n=50 follow-up:	hydrocortisone 100 mg IV then streptokinase IV 250,000 U over 30 minutes, then 100,000 U/hour titrated for 72 hours. Followed by IV heparin titrated over 7 days versus IV heparin 150 U/kg loading dose then titrated for 10 days	patients with venographically confirmed DVT duration <14 days	Parallel groups single blind US
<b>Elsharawy , 2002</b> n=35 follow-up:	catheter-directed thrombolysis with streptokinase using popliteal approach. versus heparin IV bolus 5000 U, then adjusted continuous infusion. Warfarin begun the same evening	iliofemoral venous thrombosis confirmed by duplex or venography duration <10 days	Parallel groups single blind Egypt
<b>Schulman , 1986</b> n=38 follow-up:	streptokinase 50,000 IU IV over 15 minutes then 100,000 IU over 12 hours for up to 7 days, titrated. Given with 5000 IU heparin IV over 12 hours. Warfarin begun after streptokinase ended versus heparin 5000 IU IV bolus then 30,000 IU per day, titrated for 7 days. Warfarin begun simultaneously	patients with venographically confirmed calf vein thrombosis of duration <7 days.	Parallel groups single blind Sweden

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>Tsapogas , 1973</b> n=34 follow-up:	titrated dose of streptokinase IV into ankle vein/mage/pj versus heparin IV into affected limb	patients with DVT confirmed by venogram of duration <5 days.	Parallel groups open US
<b>Kakkar (streptokinase) , 1969</b> n=NA follow-up:	streptokinase 500,000 U IV over 30 minutes, 900,000 U every 6 hours for 5 days versus heparin 10,000 U over 5 minutes, then 10,000 to 15,000 U every 6 hours for 5 days	patients with venographically confirmed DVT of leg of duration <4 days	Parallel groups single blind UK
<b>Schweizer (systemic SK) , 2000</b> n=NA follow-up:	Systemic streptokinase 3,000,000 U/day over 6 hours in conjunction with heparin for up to 7 days. Premedication: hydrocortisone 100 mg, ranitidine 50 mg, clemastine 2 mg versus heparin IV, adjusted	patients with thrombosis of popliteal or more proximal veins confirmed by venogram at more than one level of duration <9 days	Parallel groups single blind Germany
<b>tPA vs no fibrinolysis</b>			
<b>Goldhaber (tPA alone) , 1990</b> n=NA follow-up:	tPA alone 0.05 mg/kg/hour IV over 24 hours, then heparin 100U/kg bolus, then 1000 U/hour, adjusted versus heparin alone 100 U/kg bolus, then 1000 U/hour	venographically documented DVT, in popliteal or more proximal veins <14 days duration	Parallel groups single blind US
<b>Schweizer (local tPA) , 2000</b> n=NA follow-up:	local tPA 20 mg/day, over 4 hours via pedal vein for 4-7 days. IV heparin given simultaneously at 1000 IU/hour, adjusted versus heparin IV, adjusted	patients with thrombosis of popliteal or more proximal veins confirmed by venogram at more than one level of duration <9 days	Parallel groups single blind Germany
<b>Turpie , 1990</b> n=83 follow-up:	tPA + IV heparin versus 5000 U bolus then 30,000 U/24 hours, adjusted for 7-10 days (+placebo)	patients with venographically confirmed proximal DVT of lower limb of duration <7 days	Parallel groups double blind Canada
<b>Verhaeghe (high dose) , 1989</b> n=NA follow-up:	IV tPA 100 mg on day 1, 50 mg tPA on day 2. 10% of dose given as bolus; heparin 5000 U IV bolus then continuous infusion of 1000 U per hour for up to 72 hours versus heparin 5000 U IV bolus then continuous infusion of 1000 U per hour for up to 72 hours (+placebo)	hospitalised patients with DVT of popliteal or more proximal veins of the lower leg, confirmed by venography of duration <10 days.	Parallel groups double blind France, Belgium, Switzerland

continued...



<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
Goldhaber (tPA+heparin) , 1990 n=NA follow-up:	tPA 0.05 mg/kg/hour IV over 24 hours and heparin 100U/kg bolus, then 1000 U/hour, adjusted versus heparin alone 100 U/kg bolus, then 1000 U/hour.	patients with venographically documented DVT, in popliteal or more proximal veins <14 days duration	Parallel groups single blind US
Verhaeghe (low dose) , 1989 n=NA follow-up:	IV tPA 50 mg on day 1, repeated on day 2. 10% of dose given as bolus; heparin 5000 U IV bolus then continuous infusion of 1000 U per hour for up to 72 hours versus heparin 5000 U IV bolus then continuous infusion of 1000 U per hour for up to 72 hours (+placebo)	hospitalised patients with DVT of popliteal or more proximal veins of the lower leg, confirmed by venography of duration <10 days.	Parallel groups double blind France, Belgium, Switzerland
<b>tPA+heparin vs no fibrinolysis</b>			
Schweizer tPA , 1998 n=NA follow-up:	tPA 20 mg IV into pedal vein over 4 hours each day for 7 days. Heparin IV given concomitantly, with adjustment versus heparin IV, adjusted for 7 days	patients with venographically confirmed DVT of leg duration <7 days.	Parallel groups single blind Germany
<b>urokinase vs no fibrinolysis</b>			
Kiil , 1981 n=20 follow-up:	urokinase 200,000 U IV over 24 hours. After 18 hours, heparin loading dose of 15,000 units then 40,000 U/day for 5 days (+placebo) versus heparin 40,000 U/day IV for 6 days (+placebo)	patients with venographically confirmed DVT duration <72 hours	Parallel groups Double blind Denmark
Schweizer (urokinase) , 1998 n=NA follow-up:	Urokinase 100,000 IU/hr IV into pedal vein continuously for 7 days. Heparin IV for 7 days. Plasminogen monitored. Warfarin from day 7 to 12 monthsd=132 versus heparin IV, adjusted for 7 days	patients with venographically confirmed DVT of leg duration <7 days	Parallel groups single blind Germany
Schweizer (local urokinase) , 2000 n=NA follow-up:	Local urokinase 100,000 IU/day infused continuously. Fibrinogen and plasminogen monitored. Heparin IV given concomitantly versus heparin IV, adjusted	patients with thrombosis of popliteal or more proximal veins confirmed by venogram at more than one level of duration <9 days	Parallel groups single blind Germany

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>Schweizer (systemic urokinase) , 2000</b> n=NA follow-up:	Systemic urokinase 5,000,000 IU/day over 4 hours for up to 7 days. IV heparin given concomitantly versus heparin IV, adjusted	patients with thrombosis of popliteal or more proximal veins confirmed by venogram at more than one level of duration <9 days	Parallel groups single blind Germany
<b>caval filter vs no filter</b>			
<b>PREPIC , 1998</b> n=200/200 follow-up: 12 days and 2 years	caval filter versus no filter	patients with documented proximal DVT or PE, and considered high risk for pulmonary embolism	Parallel groups open
<b>apixaban 2.5mg vs placebo</b>			
<b>AMPLIFY EXT 2.5mg , 2013</b> n=842/829 follow-up:	apixaban (2.5 mg and 5 mg, twice daily) versus placebo	patients with venous thromboembolism who had completed 6 to 12 months of anticoagulation therapy	
<b>apixaban 5mg vs placebo</b>			
<b>AMPLIFY EXT 5mg , 2013</b> n=815/829 follow-up:	apixaban (2.5 mg and 5 mg, twice daily) versus placebo	patients with venous thromboembolism who had completed 6 to 12 months of anticoagulation therapy	
<b>aspirin vs placebo</b>			
<b>ASPIRE , 2012</b> n=411/411 follow-up: 37.2 months median	aspirin, at a dose of 100 mg daily, for up to 4 years versus placebo	patients who had completed initial anticoagulant therapy after a first episode of unprovoked venous thromboembolism	
<b>WARFASA , 2012</b> n=205/197 follow-up:	aspirin, 100 mg daily for 2 years versus placebo	patients with first-ever unprovoked venous thromboembolism who had completed 6 to 18 months of oral anticoagulant treatment	
<b>dabigatran vs placebo</b>			
<b>RESONATE , 2013</b> n=681/662 follow-up:	dabigatran at a dose of 150 mg twice daily versus placebo	-	
<b>heparin+warfarin vs placebo</b>			
<b>Ott import , 1998</b> n=11/12	anticoagulants (s.c. heparin followed by oral warfarin) (duration NA) versus s.c. saline followed by oral placebo tablets	-	double blind Denmark
<b>idraparinux vs placebo</b>			

continued...

Trial	Treatments	Patients	Trials design and methods
Van Gogh , 2007 [NCT00071279] n=594/621 follow-up:	once-weekly injections of 2.5 mg of idraparinux for 6 months without monitoring versus placebo	patients who had completed 6 months of prophylaxis with idraparinux or a vitamin K antagonist and in whom extended anticoagulation was warranted	Parallel groups double-blind

More details and results :

- fibrinolysis for venous thrombosis in all type of patients at <http://www.trialresultscenter.org/go-Q100>
- antithrombotics for venous thrombosis in all type of patients at <http://www.trialresultscenter.org/go-Q101>
- antithrombotics for venous thrombosis in patients with cancer at <http://www.trialresultscenter.org/go-Q103>
- caval filter for venous thrombosis in all type of patients at <http://www.trialresultscenter.org/go-Q122>
- antithrombotics for venous thrombosis in secondary prevention of VTE at <http://www.trialresultscenter.org/go-Q149>
- LMWH for venous thrombosis in all type of patients at <http://www.trialresultscenter.org/go-Q203>
- heparin (UFH or LMWH) for venous thrombosis in all type of patients at <http://www.trialresultscenter.org/go-Q204>
- UFH for venous thrombosis in all type of patients at <http://www.trialresultscenter.org/go-Q205>
- direct factor Xa inhibitors for venous thrombosis in all type of patients at <http://www.trialresultscenter.org/go-Q372>
- direct oral anticoagulant (DAO) for venous thrombosis in all types of patients at <http://www.trialresultscenter.org/go-Q505>
- antithrombotics for venous thrombosis in secondary prevention - 2 at <http://www.trialresultscenter.org/go-Q682>

## References

### RE-MEDY, 2011:

Schulman S, Kearon C, Kakkar AK, Schellong S, Eriksson H, Baanstra D, Kvamme AM, Friedman J, Mismetti P, Goldhaber SZ Extended use of dabigatran, warfarin, or placebo in venous thromboembolism. *N Engl J Med* 2013 Feb 21;368:709-18 [23425163] 10.1056/NEJMoa1113697

### REMEDY, 2013:

Schulman S, Kearon C, Kakkar AK, Schellong S, Eriksson H, Baanstra D, Kvamme AM, Friedman J, Mismetti P, Goldhaber SZ Extended use of dabigatran, warfarin, or placebo in venous thromboembolism. *N Engl J Med* 2013 Feb 21;368:709-18 [23425163]

### Veiga, 2000:

Veiga F, Escrib A, Maluenda MP, Lpez Rubio M, Margalet I, Lezana A, Gallego J, Ribera JM Low molecular weight heparin (enoxaparin) versus oral anticoagulant therapy (acenocoumarol) in the long-term treatment of deep venous thrombosis in the elderly: a randomized trial. *Thromb Haemost* 2000;84:559-64 [11057850]

### Lopez-Beret, 2001:

Lpez-Beret P, Orgaz A, Fontcuberta J, Doblas M, Martinez A, Lozano G, Romero A Low molecular weight heparin versus oral anticoagulants in the long-term treatment of deep venous thrombosis. *J Vasc Surg* 2001;33:77-90 [11137927]

### Lopaciuk, 1999:

Lopaciuk S, Bielska-Falda H, Noszczyk W, Bielawiec M, Witkiewicz W, Filipecki S, Michalak J, Ciesielski L, Mackiewicz Z, Czestochowska E, Zawilska K, Cencora A Low molecular weight heparin versus acenocoumarol in the secondary prophylaxis of deep vein thrombosis. *Thromb Haemost* 1999;81:26-31 [9974369]

### Romera, 2009:

Romera A, Cairols MA, Vila-Coll R, Mart X, Colom E, Bonell A, Lapiedra O A randomised open-label trial comparing long-term sub-cutaneous low-molecular-weight heparin compared with oral-anticoagulant therapy in the treatment of deep venous thrombosis. *Eur J Vasc Endovasc Surg* 2009;37:349-56 [19121589]

### EINSTEIN CHOICE (10mg), 2017:

Weitz JI, Lensing AWA, Prins MH, Bauersachs R, Beyer-Westendorf J, Bounameaux H, Brighton TA, Cohen AT, Davidson BL, Decousus H, Freitas MCS, Holberg  
Rivaroxaban or Aspirin for Extended Treatment of Venous Thromboembolism. *N. Engl. J. Med.* 2017; 376:1211-1222 [28316279] [10.1056/NEJMoa1700518](https://doi.org/10.1056/NEJMoa1700518)

#### **AUREC FVII, 2009:**

Eischer L, Gartner V, Schulman S, Kyrle PA, Eichinger S 6 versus 30 months anticoagulation for recurrent venous thrombosis in patients with high factor VIII. *Ann Hematol* 2009;88:485-90 [18931845] [10.1007/s00277-008-0626-1](https://doi.org/10.1007/s00277-008-0626-1)

#### **DACUS (Siragusa), 2008:**

Siragusa S, Malato A, Anastasio R, Cigna V, Milio G, Amato C, Bellisi M, Attanzio MT, Cormaci O, Pellegrino M, Dolce A, Casuccio A, Bajardi G, Mariani G  
Residual vein thrombosis to establish duration of anticoagulation after a first episode of deep vein thrombosis: the Duration of Anticoagulation based on Compression  
UltraSonography (DACUS) study. *Blood* 2008;112:511-5 [18497320] [10.1182/blood-2008-01-131656](https://doi.org/10.1182/blood-2008-01-131656)

#### **DURAC II, 1997:**

Schulman S, Granqvist S, Holmström M, Carlsson A, Lindmarker P, Nicol P, Eklund SG, Nordlander S, Lrfars G, Leijd B, Linder O, Loogna E The duration of oral  
anticoagulant therapy after a second episode of venous thromboembolism. The Duration of Anticoagulation Trial Study Group. *N Engl J Med* 1997;336:393-8 [9010144]  
[10.1056/NEJM199702063360601](https://doi.org/10.1056/NEJM199702063360601)

#### **PROLONG (Palarati), 2006:**

Palareti G, Cosmi B, Legnani C, Tosetto A, Brusi C, Iorio A, Pengo V, Ghirarduzzi A, Pattacini C, Testa S, Lensing AW, Tripodi A D-dimer testing to determine  
the duration of anticoagulation therapy. *N Engl J Med* 2006;355:1780-9 [17065639]

#### **WODIT DVT, 2001:**

Agnelli G, Prandoni P, Santamaria MG, Bagatella P, Iorio A, Bazzan M, Moia M, Guazzaloca G, Bertoldi A, Tomasi C, Scannapieco G, Ageno W Three months  
versus one year of oral anticoagulant therapy for idiopathic deep venous thrombosis. Warfarin Optimal Duration Italian Trial Investigators. *N Engl J Med* 2001;345:165-9  
[11463010] [10.1056/NEJM200107193450302](https://doi.org/10.1056/NEJM200107193450302)

#### **WODIT PE, 2003:**

Agnelli G, Prandoni P, Becattini C, Silingardi M, Taliani MR, Miccio M, Imberti D, Poggio R, Ageno W, Pogliani E, Porro F, Zonzin P Extended oral anticoagulant  
therapy after a first episode of pulmonary embolism. *Ann Intern Med* 2003;139:19-25 [12834314]

#### **DDOAT2006, :**

ongoing trial NCT00895505

#### **Vitotec, 2009:**

Vtovec M, Goln L, Roztocil K, Linhart A The development of persistent thrombotic masses in patients with deep venous thrombosis randomized to long-term  
anticoagulation treatment. *Vasa* 2009;38:238-44 [19736635] [10.1024/0301-1526.38.3.238](https://doi.org/10.1024/0301-1526.38.3.238)

#### **Gonzlez-Fajardo, 2008:**

Gonzlez-Fajardo JA, Martin-Pedrosa M, Castrodeza J, Tamames S, Vaquero-Puerta C Effect of the anticoagulant therapy in the incidence of post-thrombotic  
syndrome and recurrent thromboembolism: Comparative study of enoxaparin versus coumarin. *J Vasc Surg* 2008;48:953-9 [18639417]

#### **Wells (subgroup), 2005:**

Wells PS, Anderson DR, Rodger MA, Forgie MA, Florack P, Touchie D, Morrow B, Gray L, O'Rourke K, Wells G, Kovacs J, Kovacs MJ A randomized trial comparing  
2 low-molecular-weight heparins for the outpatient treatment of deep vein thrombosis and pulmonary embolism. *Arch Intern Med* 2005;165:733-8 [15824291]

#### **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](https://doi.org/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](https://doi.org/10.1056/NEJMoa1207541)

#### **WARFASA, 2012:**

Becattini C, Agnelli G, Schenone A, Eichinger S, Bucherini E, Silingardi M, Bianchi M, Moia M, Ageno W, Vandelli MR, Grandone E, Prandoni P Aspirin for  
preventing the recurrence of venous thromboembolism. *N Engl J Med* 2012 May 24;366:1959-67 [22621626] [10.1056/NEJMoa1114238](https://doi.org/10.1056/NEJMoa1114238)

#### **ASPIRE, 2012:**

Brighton TA, Eikelboom JW, Mann K, Mister R, Gallus A, Ockelford P, Gibbs H, Hague W, Xavier D, Diaz R, Kirby A, Simes J Low-dose aspirin for preventing recurrent venous thromboembolism. *N Engl J Med* 2012;367:1979-87 [[23121403](#)]

**RE-SONATE, 2011:**

**VanGogh extension, 2007:**

Buller HR, Cohen AT, Davidson B, Decousus H, Gallus AS, Gent M, Pillion G, Piovella F, Prins MH, Raskob GE *N Engl J Med* 2007 Sep 13;357:1105-12 [[17855671](#)]  
[10.1056/NEJMoa067703](#)

**EINSTEIN-extension, 2009:**

Buller H R. Once daily oral rivaroxaban versus placebo in the long term treatment of recurrent symptomatic venous thromboembolism. The Einstein-extension study. *ASH*, 8 dicembre 2009

Oral Rivaroxaban for Symptomatic Venous Thromboembolism. *N Engl J Med* 2010 Dec 3;: [[21128814](#)] [10.1056/NEJMoa1007903](#)

**PROLONG (Palareti), 2006:**

Palareti G, Cosmi B, Legnani C, Tostetto A, Brusi C, Iorio A, Pengo V, Ghirarduzzi A, Pattacini C, Testa S, Lensing AW, Tripodi A D-dimer testing to determine the duration of anticoagulation therapy. *N Engl J Med* 2006;355:1780-9 [[17065639](#)]

**PREVENT (Ridker), 2003:**

Ridker PM, Goldhaber SZ, Danielson E, Rosenberg Y, Eby CS, Deitcher SR, Cushman M, Moll S, Kessler CM, Elliott CG, Paulson R, Wong T, Bauer KA, Schwartz BA, Miletich JP, Bounameaux H, Glynn RJ Long-term, low-intensity warfarin therapy for the prevention of recurrent venous thromboembolism. *N Engl J Med* 2003;348:1425-34 [[12601075](#)]

**Agnelli, 2003:**

Agnelli G, Prandoni P, Becattini C, Silingardi M, Taliani MR, Miccio M, Imberti D, Poggio R, Ageno W, Pogliani E, Porro F, Zonzin P Extended oral anticoagulant therapy after a first episode of pulmonary embolism. *Ann Intern Med* 2003;139:19-25 [[12834314](#)]

**Agnelli, 2001:**

Agnelli G, Prandoni P, Santamaria MG, Bagatella P, Iorio A, Bazzan M, Moia M, Guazzaloca G, Bertoldi A, Tomasi C, Scannapieco G, Ageno W Three months versus one year of oral anticoagulant therapy for idiopathic deep venous thrombosis. Warfarin Optimal Duration Italian Trial Investigators. *N Engl J Med* 2001;345:165-9 [[11463010](#)]

**LAFIT (Kearon), 1999:**

Kearon C, Gent M, Hirsh J, Weitz J, Kovacs MJ, Anderson DR, Turpie AG, Green D, Ginsberg JS, Wells P, MacKinnon B, Julian JA A comparison of three months of anticoagulation with extended anticoagulation for a first episode of idiopathic venous thromboembolism. *N Engl J Med* 1999;340:901-7 [[10089183](#)]

Kearon C, Gent M, Hirsh J, Weitz J, Kovacs MJ, Anderson DR, Turpie AG, Green D, Ginsberg JS, Wells P, MacKinnon B, Julian JA A comparison of three months of anticoagulation with extended anticoagulation for a first episode of idiopathic venous thromboembolism. *N Engl J Med* 1999;340:901-7 [[10089183](#)]

**ELAET (Kearon), 2004:**

Kearon C, Ginsberg JS, Anderson DR, Kovacs MJ, Wells P, Julian JA, Mackinnon B, Demers C, Douketis J, Turpie AG, Van Nguyen P, Green D, Kassis J, Kahn SR, Solymoss S, Desjardins L, Geerts W, Johnston M, Weitz JI, Hirsh J, Gent M Comparison of 1 month with 3 months of anticoagulation for a first episode of venous thromboembolism associated with a transient risk factor. *J Thromb Haemost* 2004;2:743-9 [[15099280](#)]

**Levine, 1995:**

Levine MN, Hirsh J, Gent M, Turpie AG, Weitz J, Ginsberg J, Geerts W, LeClerc J, Neemeh J, Powers P Optimal duration of oral anticoagulant therapy: a randomized trial comparing four weeks with three months of warfarin in patients with proximal deep vein thrombosis. *Thromb Haemost* 1995;74:606-11 [[8584992](#)]

**DURAC (Schulman), 1997:**

Schulman S, Granqvist S, Holmström M, Carlsson A, Lindmarker P, Nicol P, Eklund SG, Nordlander S, Lrfars G, Leijd B, Linder O, Loogna E The duration of oral anticoagulant therapy after a second episode of venous thromboembolism. The Duration of Anticoagulation Trial Study Group. *N Engl J Med* 1997;336:393-8 [[9010144](#)]

**THRIVE III, 2003:**

Schulman S, Whlander K, Lundström T, Clason SB, Eriksson H Secondary prevention of venous thromboembolism with the oral direct thrombin inhibitor ximelagatran. *N Engl J Med* 2003 Oct 30;349:1713-21 [[14585939](#)]

Schulman S, Lundström T, Wlander K, Billing Clason S, Eriksson H Ximelagatran for the secondary prevention of venous thromboembolism: a complementary follow-up analysis of the THRIVE III study. *Thromb Haemost* 2005 Oct;94:820-4 [[16270637](#)]

**ELATE, 2003:**

Kearon C, Ginsberg JS, Kovacs MJ, Anderson DR, Wells P, Julian JA, MacKinnon B, Weitz JI, Crowther MA, Dolan S, Turpie AG, Geerts W, Solymoss S, van Nguyen P, Demers C, Kahn SR, Kassis J, Rodger M, Hambleton J, Gent M Comparison of low-intensity warfarin therapy with conventional-intensity warfarin therapy for long-term prevention of recurrent venous thromboembolism. *N Engl J Med* 2003;349:631-9 [[12917299](#)] [10.1056/NEJMoa035422](#)

**Kakkar (arvin), 1969:**

**Arneson, 1978:**

Arnesen H, Heilo A, Jakobsen E, Ly B, Skaga E A prospective study of streptokinase and heparin in the treatment of deep vein thrombosis. *Acta Med Scand* 1978;203:457-63 [[352099](#)]

Arnesen H, Hiseth A, Ly B Streptokinase of heparin in the treatment of deep vein thrombosis. Follow-up results of a prospective study. *Acta Med Scand* 1982;211:65-8 [[7041523](#)]

**Common, 1976:**

Common HH, Seaman AJ, Rsch J, Porter JM, Dotter CT Deep vein thrombosis treated with streptokinase or heparin. Follow-up of a randomized study. *Angiology* 1976;27:645-54 [[802925](#)]

Porter JM, Seaman AJ, Common HH, Rsch J, Eidemiller LR, Calhoun AD Comparison of heparin and streptokinase in the treatment of venous thrombosis. *Am Surg* 1975;41:511-19 [[1101755](#)]

Rsch J, Dotter CT, Seaman AJ, Porter JM, Common HH Healing of deep venous thrombosis: venographic findings in a randomized study comparing streptokinase and heparin. *AJR Am J Roentgenol* 1976;127:553-8 [[970521](#)]

Seaman AJ, Common HH, Rsch J, Dotter CT, Porter JM, Lindell TD, Lawler WL, Schlueter WJ Deep vein thrombosis treated with streptokinase or heparin. A randomized study. *Angiology* 1976;27:549-56 [[1053467](#)]

**Elsharawy, 2002:**

Elsharawy M, Elzayat E Early results of thrombolysis vs anticoagulation in iliofemoral venous thrombosis. A randomised clinical trial. *Eur J Vasc Endovasc Surg* 2002;24:209-14 [[12217281](#)]

**Schulman, 1986:**

Schulman S, Granqvist S, Juhlin-Dannfelt A, Lockner D Long-term sequelae of calf vein thrombosis treated with heparin or low-dose streptokinase. *Acta Med Scand* 1986;219:349-57 [[3521207](#)]

**Tsapogas, 1973:**

Tsapogas MJ, Peabody RA, Wu KT, Karmody AM, Devaraj KT, Eckert C Controlled study of thrombolytic therapy in deep vein thrombosis. *Surgery* 1973;74:973-84 [[4749637](#)]

**Kakkar (streptokinase), 1969:**

**Schweizer (systemic SK), 2000:**

Schweizer J, Kirch W, Koch R, Elix H, Hellner G, Forkmann L, Graf A Short- and long-term results after thrombolytic treatment of deep venous thrombosis. *J Am Coll Cardiol* 2000;36:1336-43 [[11028492](#)]

**Goldhaber (tPA alone), 1990:**

Goldhaber SZ, Meyerovitz MF, Green D, Vogelzang RL, Citrin P, Heit J, Sobel M, Wheeler HB, Plante D, Kim H Randomized controlled trial of tissue plasminogen activator in proximal deep venous thrombosis. *Am J Med* 1990;88:235-40 [[2106783](#)]

**Schweizer (local tPA), 2000:**

Schweizer J, Kirch W, Koch R, Elix H, Hellner G, Forkmann L, Graf A Short- and long-term results after thrombolytic treatment of deep venous thrombosis. *J Am Coll Cardiol* 2000;36:1336-43 [[11028492](#)]

**Turpie, 1990:**

Turpie AG, Levine MN, Hirsh J, Ginsberg JS, Cruickshank M, Jay R, Gent M Tissue plasminogen activator (rt-PA) vs heparin in deep vein thrombosis. Results of a randomized trial. *Chest* 1990;97:172S-175S [[2108855](#)]

Hirsh J. Thrombolytic therapy for venous thrombosis and pulmonary embolism *Thrombosis Haemostasis* 1989;62(1):547-Abstract No 1739

**Verhaeghe (high dose), 1989:**

Verhaeghe R, Besse P, Bounameaux H, Marbet GA Multicenter pilot study of the efficacy and safety of systemic rt-PA administration in the treatment of deep vein thrombosis of the lower extremities and/or pelvis. *Thromb Res* 1989;55:5-11 [[2506661](#)]

**Goldhaber (tPA+heparin), 1990:**

Goldhaber SZ, Meyerovitz MF, Green D, Vogelzang RL, Citrin P, Heit J, Sobel M, Wheeler HB, Plante D, Kim H Randomized controlled trial of tissue plasminogen activator in proximal deep venous thrombosis. *Am J Med* 1990;88:235-40 [2106783]

**Verhaeghe (low dose), 1989:**

Verhaeghe R, Besse P, Bounameaux H, Marbet GA Multicenter pilot study of the efficacy and safety of systemic rt-PA administration in the treatment of deep vein thrombosis of the lower extremities and/or pelvis. *Thromb Res* 1989;55:5-11 [2506661]

**Schweizer tPA, 1998:**

Schweizer J, Elix H, Altmann E, Hellner G, Forkmann L Comparative results of thrombolysis treatment with rt-PA and urokinase: a pilot study. *Vasa* 1998;27:167-71 [9747153]

**Kiil, 1981:**

Kiil J, Carvalho A, Saks P, Nielsen HO Urokinase or heparin in the management of patients with deep vein thrombosis? *Acta Chir Scand* 1981;147:529-32 [7048826]

**Schweizer (urokinase), 1998:**

Schweizer J, Elix H, Altmann E, Hellner G, Forkmann L Comparative results of thrombolysis treatment with rt-PA and urokinase: a pilot study. *Vasa* 1998;27:167-71 [9747153]

**Schweizer (local urokinase), 2000:**

Schweizer J, Kirch W, Koch R, Elix H, Hellner G, Forkmann L, Graf A Short- and long-term results after thrombolytic treatment of deep venous thrombosis. *J Am Coll Cardiol* 2000;36:1336-43 [11028492]

**Schweizer (systemic urokinase), 2000:**

Schweizer J, Kirch W, Koch R, Elix H, Hellner G, Forkmann L, Graf A Short- and long-term results after thrombolytic treatment of deep venous thrombosis. *J Am Coll Cardiol* 2000;36:1336-43 [11028492]

**PREPIC, 1998:**

Decusus H, Leizorovicz A, Parent F, Page Y, Tardy B, Girard P, Laporte S, Faivre R, Charbonnier B, Barral FG, Huet Y, Simonneau G A clinical trial of vena caval filters in the prevention of pulmonary embolism in patients with proximal deep-vein thrombosis. Prevention du Risque d'Embolie Pulmonaire par Interruption Cave Study Group. *N Engl J Med* 1998;338:409-15 [9459643]

Eight-year follow-up of patients with permanent vena cava filters in the prevention of pulmonary embolism: the PREPIC (Prevention du Risque d'Embolie Pulmonaire par Interruption Cave) randomized study. *Circulation* 2005;112:416-22 [16009794]

**AMPLIFY EXT 2.5mg, 2013:**

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* 2013;368:699-708 [23216615] 10.1056/NEJMoa1207541

**AMPLIFY EXT 5mg, 2013:**

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* 2013;368:699-708 [23216615] 10.1056/NEJMoa1207541

**ASPIRE, 2012:**

Brighton TA, Eikelboom JW, Mann K, Mister R, Gallus A, Ockelford P, Gibbs H, Hague W, Xavier D, Diaz R, Kirby A, Simes J Low-dose aspirin for preventing recurrent venous thromboembolism. *N Engl J Med* 2012;367:1979-87 [23121403] 10.1056/NEJMoa1210384

**WARFASA, 2012:**

Becattini C, Agnelli G, Schenone A, Eichinger S, Bucherini E, Silingardi M, Bianchi M, Moia M, Ageno W, Vandelli MR, Grandone E, Prandoni P Aspirin for preventing the recurrence of venous thromboembolism. *N Engl J Med* 2012;366:1959-67 [22621626] 10.1056/NEJMoa1114238

**RESONATE, 2013:**

Schulman S, Kearon C, Kakkar AK, Schellong S, Eriksson H, Baanstra D, Kvanne AM, Friedman J, Mismetti P, Goldhaber SZ Extended use of dabigatran, warfarin, or placebo in venous thromboembolism. *N Engl J Med* 2013;368:709-18 [23425163] 10.1056/NEJMoa1113697

**Ott import, 1998:**

Ott P, Eldrup E, Oxholm P [Value of anticoagulant therapy in deep venous thrombosis in the lower limb in elderly, mobilized patients. A double-blind placebo controlled study with open therapeutic guidance] *Ugeskr Laeger* 1988;150:218-21 [3287734]

**Van Gogh, 2007:**



Buller HR, Cohen AT, Davidson B, Decousus H, Gallus AS, Gent M, Pillion G, Piovella F, Prins MH, Raskob GE Extended prophylaxis of venous thromboembolism with idraparin. N Engl J Med 2007;357:1105-12 [[17855671](#)] [10.1056/NEJMoa067703](#)

## 15 abdominal aortic aneurysm

Trial	Treatments	Patients	Trials design and methods
<b>endovascular repair vs surveillance</b>			
<b>PIVOTAL (Ouriel) , 2010</b> n=366/362 follow-up: 20 months	early endovascular repair versus ultrasound surveillance	patients (13.3% women; mean age, 71 +/- 8 years) with 4 to 5 cm abdominal aortic aneurysms	Parallel groups open USA
<b>EVAR trial 2 , 2005</b> [ISRCTN55703451] n=197/207 follow-up: 2.4 y (median)	Endovascular aneurysm repair versus No intervention	patients aged 60 years or older who had aneurysms of at least 55 cm in diameter and of poor health status considered unfit for major surgery.	Parallel groups open UK
<b>endovascular repair vs open repair</b>			
<b>OVER , 2009</b> [NCT00094575] n=444/437 follow-up: 1.8y	endovascular repair versus open repair	men (aged >=49 years) with abdominal aortic aneurysms candidate for both both elective endovascular repair and open repair	Parallel groups open USA
<b>DREAM , 2005</b> [NCT00421330] n=173/178 follow-up: 2 y (6 y)	elective endovascular repair versus conventional open repair	abdominal aortic aneurysm of at least 5 cm in diameter and who were considered suitable candidates for both techniques.	Parallel groups open The Netherlands
<b>EVAR trial 1 , 2005</b> [ISRCTN55703451] n=626/626 follow-up: 2.9 y (median)	endovascular aneurysm repair versus open repair	aneurysms of at least 55 cm in diameter	Parallel groups open UK

More details and results :

- endovascular treatment for abdominal aortic aneurysm in all type of patients at <http://www.trialresultscenter.org/go-Q356>
- endovascular treatment for abdominal aortic aneurysm in patient with large AAA at <http://www.trialresultscenter.org/go-Q419>
- endovascular treatment for abdominal aortic aneurysm in patients with small AAA at <http://www.trialresultscenter.org/go-Q420>

## References

### PIVOTAL (Ouriel), 2010:

Ouriel K, Clair DG, Kent KC, Zarins CK Endovascular repair compared with surveillance for patients with small abdominal aortic aneurysms. J Vasc Surg 2010;51:1081-7 [[20304589](#)] [10.1016/j.jvs.2009.10.113](#)

### EVAR trial 2, 2005:

Endovascular aneurysm repair and outcome in patients unfit for open repair of abdominal aortic aneurysm (EVAR trial 2): randomised controlled trial. Lancet 2005;365:2187-92 [[15978926](#)]



Greenhalgh RM, Brown LC, Powell JT, Thompson SG, Epstein D Endovascular repair of aortic aneurysm in patients physically ineligible for open repair. *N Engl J Med* 2010 May 20;362:1872-80 [20382982] [10.1056/NEJMoa0911056](https://doi.org/10.1056/NEJMoa0911056)

**OVER, 2009:**

Lederle FA, Freischlag JA, Kyriakides TC, Padberg FT Jr, Matsumura JS, Kohler TR, Lin PH, Jean-Claude JM, Cikrit DF, Swanson KM, Peduzzi PN Outcomes Following Endovascular vs Open Repair of Abdominal Aortic Aneurysm: A Randomized Trial. *JAMA* 2009;302:1535-1542 [19826022]

**DREAM, 2005:**

Blankensteijn JD, de Jong SE, Prinssen M, van der Ham AC, Buth J, van Sterkenburg SM, Verhagen HJ, Buskens E, Grobbee DE Two-year outcomes after conventional or endovascular repair of abdominal aortic aneurysms. *N Engl J Med* 2005;352:2398-405 [15944424]

Prinssen M, Verhoeven EL, Buth J, Cuypers PW, van Sambeek MR, Balm R, Buskens E, Grobbee DE, Blankensteijn JD A randomized trial comparing conventional and endovascular repair of abdominal aortic aneurysms. *N Engl J Med* 2004;351:1607-18 [15483279]

De Bruin JL, Baas AF, Buth J, Prinssen M, Verhoeven EL, Cuypers PW, van Sambeek MR, Balm R, Grobbee DE, Blankensteijn JD Long-term outcome of open or endovascular repair of abdominal aortic aneurysm. *N Engl J Med* 2010 May 20;362:1881-9 [20484396]

**EVAR trial 1, 2005:**

Endovascular aneurysm repair versus open repair in patients with abdominal aortic aneurysm (EVAR trial 1): randomised controlled trial. *Lancet* 2005;365:2179-86 [15978925]

Greenhalgh RM, Brown LC, Kwong GP, Powell JT, Thompson SG Comparison of endovascular aneurysm repair with open repair in patients with abdominal aortic aneurysm (EVAR trial 1), 30-day operative mortality results: randomised controlled trial. *Lancet* 2004;364:843-8 [15351191]

Greenhalgh RM, Brown LC, Powell JT, Thompson SG, Epstein D, Sculpher MJ Endovascular versus open repair of abdominal aortic aneurysm. *N Engl J Med* 2010 May 20;362:1863-71 [20382983] [10.1056/NEJMoa0909305](https://doi.org/10.1056/NEJMoa0909305)

Entry terms: enoxaparin, Lovenox, Clexane, acebutolol, Sectral, Monitan, Rhotral, Neptal, spironolactone, Veroshpiron, Verospirone, Spiractin, Spirobeta, Spirogamma, Spirolang, Spiro-no-Isis, Spiro-no Isis, Spironone, Spirospare, Verospiron, Aldactone, Aldactone A, Aquareduct, duraspiron, Espironolactona Alter, Espironolactona Mundogen, Flumach, Frumikal, Jenaspiron, Novo-Spiroton, Novo Spiroton, NovoSpiroton, Practon, Spiro L.U.T., spiro von ct, , alprenolol, amiloride, amiodarone, Amiobeta, Cordarone, Cordarex, Amiodarex, Kordaron, Trangorex, Amiodarona, Amiohexal, Braxan, Corbionax, Ortacrone, Rytmarone, Tachydaron, Aratac, amrinone, apixaban, BMS 562247, BMS562247, BMS-562247, Eliquis, , aspirin, atenolol