Clinical trials of anticoagulant for acute coronary syndrome in All ACS (including AMI)

TrialResults-center www.trialresultscenter.org

1 oral anticoagulant

Trial	Treatments	Patients	Trials design and methods
coumadin vs control (on top of aspirin)			
ASPECT-2 (coumadin+asp vs asp) , 2002 n=333/336 follow-up: 1 year	coumadin(INR mean 2.4) +aspirin versus aspirin	UA, AMI	open the Netherlands
warfarin vs control (on top of aspirin)			
ATACS (pilot study) (warfarin vs control) , 1990 n=37/32 follow-up: 65279;3 months	heparin/warfarin target INR 65279;3-4.5 + aspirin versus aspirin alone	65279;UA, NSTEMI	open
ATACS , 1994 n=105/109 follow-up: 3 months	heparin/warfarin (INR median 2.3) + aspirin versus aspirin	UA, NSTEMI	open
CARS , 1997 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	
OASIS Pilot (phase 1) , 1998 n=155/154 follow-up: 6 months	warfarin 3mg/d for 6 months (INR mean 1.5) versus control	UA, NSTEMI	open
OASIS Pilot (phase 2) , 1998 n=98/99 follow-up: 3 months	warfarin adjusted dose (INR mean 2.3) for 3 months versus standard treatment	UA, NSTEMI	open
OASIS-2 Warfarin Substudy , 2001 n=1848/1864 follow-up: 5 months	warfarin target INR 65279;22.5 for 5 months +aspirin versus control	UA	open
APRICOT-2 , 2002 n=135/139 follow-up: 3 months	moderate-intensity coumarin target INR 2-3 (+aspirin) versus aspirin	STEMI	
CHAMP , 2002 n=2522/2537 follow-up: 2.7 years	-	AMI	

continued...

Trial	Treatments	Patients	Trials design and methods
WARIS , 2002 n=1208/1206 follow-up: 4 years	-	AMI	
LoWASA , 2004 n=1659/1641 follow-up: 5 years	-	AMI	
Zibaeenezhad , 2004 n=70/70 follow-up: 1 year	-	AMI	
warfarin vs placebo (on top of aspirin)			
Williams , 1997 n=29/28 follow-up: 2.5 months	warfarin target INR 65279;22.5 +aspirin versus placebo +aspirin	UA, AMI	double blind
Huyhn , 2001 n=44/46 follow-up: 1 year	warfarin adjusted dose for INR 22.5 +aspirin versus placebo +aspirin	UA, NSTEMI with prior CABG	double blind
coumadin vs aspirin			
ASPECT-2 (coumadin vs aspirin) , 2002 n=325/336 follow-up: 1 year (range 0-26 months)	coumadin (phenprocoumon or acenocoumarol) target INR 3-4) versus aspirin 80mg daily	UA, AMI	Parallel groups open the Netherlands
warfarin vs aspirin			
ATACS (pilot study) warfarin vs aspirin , 1990 n=24/32 follow-up: 65279;3 months	heparin/warfarin target INR 65279;3-4 versus aspirin 65279;325 mg daily	65279;UA, NSTEMI	open

References

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 (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]

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]

Huyhn, 2001:

Huynh T, Throux P, Bogaty P, Nasmith J, Solymoss S Aspirin, warfarin, or the combination for secondary prevention of coronary events in patients with acute coronary syndromes and prior coronary artery bypass surgery. Circulation 2001;103:3069-74 [11425770]

ASPECT-2 (coumadin vs aspirin), 2002:

ATACS (pilot study) warfarin vs aspirin, 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]

2 oral direct thrombin inhibitor

Trial	Treatments	Patients	Trials design and methods
dabigatran vs placebo			

continued...

Trial	Treatments	Patients	Trials design and methods
REDEEM , 2009 *unpublished* [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 myocardical infarction)	Parallel groups double blind

References

REDEEM, 2009:

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]

3 oral factor Xa inhibitor

Trial	Treatments	Patients	Trials design and methods
apixaban vs placebo			
APPRAISE 2 , 2011 [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
APPRAISE-1 (10mg od) , 2009 [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
APPRAISE-1 (2.5 mg bid) , 2009 [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
APPRAISE japan *ongoing* [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
rivaroxaban 2.5mg vs placebo			
ATLAS ACS-TIMI 46 (2.5mg) , 2009 [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...

Trial	Treatments	Patients	Trials design and methods
ATLAS ACS 2 - TIMI 51 (2.5mg) , 2011 [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
rivaroxaban 5mg vs placebo			
ATLAS ACS-TIMI 46 (5mg) , 2009 [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
ATLAS ACS 2 - TIMI 51 (5mg) , 2011 [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
ximelagatran vs placebo			
ESTEEM , 2003 n=1245/638 follow-up: 6 months	oral ximelagatran at doses of 24 mg, 36 mg, 48 mg, or 60 mg twice daily versus placebo	patients who had had recent ST-elevation or non-STelevation myocardial infarction	Parallel groups double-blind
otamixaban vs unfractionated heparin			
SEPIA-ACS1 TIMI 42 , 2009 [NCT00317395] n=2792/449 follow-up: 7 days	otamixaban 5 doses (008 mg/kg bolus followed by 0.035, 0.070, 0.105, 0.140, 0.175 mg/kg/h) versus Heparin+eptifibatide	patients with non-ST-elevation acute coronary syndromes	Parallel groups double blind 36 countries

References

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

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:

APPRAISE japan, :

ATLAS ACS-TIMI 46 (2.5mg), 2009:

ATLAS ACS 2 - TIMI 51 (2.5mg), 2011:

ATLAS ACS-TIMI 46 (5mg), 2009:

ATLAS ACS 2 - TIMI 51 (5mg), 2011:

ESTEEM, 2003:

4 About TrialResults-center.org

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

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

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

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

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