

Clinical trials of angiotensin-Converting Enzyme Inhibitors for acute myocardial infarction in systematic early treatment (with or without sign of HF)

TrialResults-center www.trialresultscenter.org

1 angiotensin-converting enzyme inhibitors

Trial	Treatments	Patients	Trials design and methods
irbesartan vs control			
GLOBAL <i>ongoing</i> [NCT00125645] n=NA follow-up: 3 months	irbesartan versus usual care	patients with acute myocardial infarction, a wall motion score >1.3 (EF>0.40) and signs of diastolic dysfunction	Parallel groups open
captopril vs placebo			
Bussmann , 1992 n=22/24 follow-up: 48h	slow intravenous bolus injection of 2.5 or 5.0 mg captopril followed by a continuous infusion of 1.5-2.0 mg/h for a period of 48 hours versus placebo	patients with acute myocardial infarction	Parallel groups double blind
CATS , 1996 n=149/149 follow-up: 1 year	captopril 25 mg three times a day versus placebo	patients with a first anterior myocardial infarction treated with intravenous streptokinase within 6h of onset of symptoms	Parallel groups double blind The Netherlands
CCS-1 , 1995 n=13634 follow-up: 1 month	captopril 6.25 mg initial dose, 12.5 mg 2 h later, and then 12.5 mg three times daily for 28 days versus placebo	Acute MI <36h of MI	Parallel groups double blind China
Di Pasquale , 1997 n=31/30 follow-up: 12h	captopril first dose 2-4 h after starting thrombolysis (the dose was then increased up to 25 mg every 8 h versus placebo	patients hospitalized for suspected anterior AMI within 4 h from the onset of symptoms suitable for thrombolysis	Parallel groups double blind italy
Di Pasquale , 1994 n=188/183 follow-up: 2h	captopril, 6.25 mg, orally 15 min before thrombolysis versus placebo before thrombolysis	patients with acute myocardial infarction , hospitalized within 4 h of the onset of symptoms	Parallel groups double blind Italy
ECCE , 1997 n=104/104 follow-up: 1 month	captopril titrated dose in order to preserve their blood pressure versus placebo	patients with acute myocardial infarction	Parallel groups double blind

continued...

Trial	Treatments	Patients	Trials design and methods
French , 1999 n=243/250 follow-up: 1 year	captopril 6.25 mg, increasing to 50 mg t.d.s. versus placebo	patients aged <or = 75 years with first infarctions, presenting within 4 h of symptom onset	Parallel groups double blind New Zealand
Galcera , 1993 n=21/22 follow-up: 14 days	captopril versus placebo	patients with a first acute myocardial infarction and a pulmonary capillary pressure equal or above 17 mmHg	Parallel groups double blind
Hargreaves , 1992 n=36/36 follow-up: 28 days	12.5 mg of captopril three times daily versus placebo	patients with acute myocardial infarction (systolic blood pressure >90 mm Hg) within 24 hours of the start of pain	Parallel groups double blind UK
ISIS-4 , 1995 n=29028/29022 follow-up: 1 month	captopril 6.25mg twice daily initially titrated up to 50 mg twice daily (for 1 month) versus placebo	Acute MI <24h of MI, no cardiogenic shock or persistent severe hypotension	Factorial plan double blind 31 countries
Nabel , 1991 n=20/18 follow-up: 3 months	intravenous followed by oral captopril versus placebo	patients with myocardial infarction	Parallel groups double blind
Ray , 1993 n=99 follow-up: 1 year	captopril 25 mg three times a day versus placebo	haemodynamically stable patients with acute myocardial infarction, selected on clinical grounds as being at risk of late ventricular dilatation	Parallel groups double blind Glasgow
Sharpe , 1991 n=100 follow-up: 3 months	captopril 50 mg twice daily versus placebo	patients with Q wave myocardial infarction, but without clinical heart failure 24-48h after onset of symptoms	Parallel groups double blind
captopril or enalapril vs placebo			
PRACTICAL (captopril) , 1994 n=150/75 follow-up: 1 year	captopril 25 mg three times daily or enalapril 5 mg three times daily versus placebo	patients with acute myocardial infarction within 24 hours of onset	Parallel groups double blind
enalapril vs placebo			
CONSENSUS 2 , 1992 n=3044/3046 follow-up: 6 months	enalapril (1 mg IV infusion +5-20 mg PO daily) for 6 months versus placebo	patients with acute myocardial infarctions and blood pressure above 100/60 mm Hg, <24h of MI	Parallel groups double blind Scandinavia
Schulman , 1995 n=22/21 follow-up: 1 year	intravenous enalaprilat (1 mg) then oral treatment for 1 month versus placebo	patients with an acute Q-wave AMI within 24 hours of symptom onset	Parallel groups double blind US
fosinopril vs placebo			
FAMIS , 1998 n=142/143 follow-up: 2 years	fosinopril versus placebo	patients with anterior acute myocardial infarction within 9 hours of onset	Parallel groups double blind Italy
lisinopril vs placebo			

continued...

Trial	Treatments	Patients	Trials design and methods
GISSI 3 , 1994 n=9435/9460 follow-up: 6 months	lisinopril (5 mg initial dose and then 10 mg daily) for 42 days versus open control	Acute MI <24h of MI	Factorial plan open Italy
ramipril vs placebo			
Wagner , 2002 n=51/48 follow-up: 7 days	2.5 mg ramipril orally prior to thrombolysis and 12 h later versus placebo	patients with acute myocardial infarction	Parallel groups double blind
zofenopril vs placebo			
SMILE , 1995 n=772/784 follow-up: 1 year	zofenopril initial dose 7.5 mg, up to a target dose of 30mg twice daily versus placebo	patients within 24 hours after a acute anterior myocardial infarction who were not undergoing thrombolysis	Parallel groups double blind Italy

References

GLOBAL, :

Bussmann, 1992:

Bussmann WD, Micke G, Hildenbrand R, Klepzig H Jr [Captopril in acute myocardial infarct: its effect on infarct size and arrhythmias] Dtsch Med Wochenschr 1992;117:651-7 [1572248]

CATS, 1996:

van Gilst WH, Kingma JH, Peels KH, Dambrink JH, St John Sutton M Which patient benefits from early angiotensin-converting enzyme inhibition after myocardial infarction? Results of one-year serial echocardiographic follow-up from the Captopril and Thrombolysis Study (CATS). J Am Coll Cardiol 1996;28:114-21 [8752803]

CCS-1, 1995:

Oral captopril versus placebo among 13,634 patients with suspected acute myocardial infarction: interim report from the Chinese Cardiac Study (CCS-1) Lancet 1995 Mar 18;345:686-7 [7885123]

Di Pasquale, 1997:

Di Pasquale P, Bucca V, Scalzo S, Cannizzaro S, Longo AM, Alessi V, D'Amato M, Manusia F, Magatti MF [Is the reduction of the plasma levels of endothelin in the acute and sub-acute stage of myocardial infarct one of the beneficial effects of early treatment with ace inhibitors?] G Ital Cardiol 1996;26:673-80 [8803588]

Di Pasquale P, Valdes L, Albano V, Bucca V, Scalzo S, Pieri D, Maringhini G, Paterna S Early captopril treatment reduces plasma endothelin concentrations in the acute and subacute phases of myocardial infarction: a pilot study. J Cardiovasc Pharmacol 1997;29:202-8 [9057069]

Di Pasquale P, Bucca V, Scalzo S, Cannizzaro S, Longo AM, Alessi V, D'Amato M, Manusia F, Magatti MF [Is the reduction of the plasma levels of endothelin in the acute and sub-acute stage of myocardial infarct one of the beneficial effects of early treatment with ace inhibitors?] G Ital Cardiol 1996;26:673-80 [8803588]

Di Pasquale, 1994:

Di Pasquale P, Paterna S, Bucca V, Maringhini G, Magatti M Effects of the administration of captopril, metoprolol and of the captopril-metoprolol combination as adjuvant therapy during thrombolysis in acute myocardial infarction. Int J Cardiol 1994;46:107-12 [7814158]

Di Pasquale P, Paterna S, Cannizzaro S, Bucca V Does captopril treatment before thrombolysis in acute myocardial infarction attenuate reperfusion damage? Short-term and long-term effects. Int J Cardiol 1994;43:43-50 [8175218]

Di Pasquale P, Paterna S, Parrinello G, Bucca V, Cannizzaro S, Pipitone F, Maringhini G, Scalzo S, Licata G Captopril does not affect plasma endothelin-1 during thrombolysis and reperfusion. Int J Cardiol 1995;51:131-5 [8522408]

ECCE, 1997:

Kleber FX, Sabin GV, Winter UJ, Reindl I, Beil S, Wenzel M, Fischer M, Doering W Angiotensin-converting enzyme inhibitors in preventing remodeling and development of heart failure after acute myocardial infarction: results of the German multicenter study of the effects of captopril on cardiopulmonary exercise parameters (ECCE). *Am J Cardiol* 1997;80:162A-167A [[9293972](#)]

French, 1999:

French JK, Amos DJ, Williams BF, Cross DB, Elliott JM, Hart HH, Williams MG, Norris RM, Ashton NG, Whitlock RM, McLaughlin SC, White HD Effects of early captopril administration after thrombolysis on regional wall motion in relation to infarct artery blood flow. *J Am Coll Cardiol* 1999;33:139-45 [[9935020](#)]

Galcera, 1993:

Galcera-Tomas J, Nuo de la Rosa JA, Torres-Martinez G, Rodriguez-Garcia P, Castillo-Soria FJ, Canton-Martinez A, Campos-Peris JV, Pico-Aracil F, Ruiz-Ros JA, Ruiperez-Abizanda JA Effects of early use of captopril on haemodynamics and short-term ventricular remodelling in acute anterior myocardial infarction. *Eur Heart J* 1993;14:259-66 [[8449203](#)]

Hargreaves, 1992:

Hargreaves AD, Kolettis T, Jacob AJ, Flint LL, Turnbull LW, Muir AL, Boon NA Early vasodilator treatment in myocardial infarction: appropriate for the majority or minority? *Br Heart J* 1992;68:369-73 [[1449918](#)]

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 Mar 18;345:669-85 [[7661937](#)]

Nabel, 1991:

Nabel EG, Topol EJ, Galeana A, Ellis SG, Bates ER, Werns SW, Walton JA, Muller DW, Schwaiger M, Pitt B A randomized placebo-controlled trial of combined early intravenous captopril and recombinant tissue-type plasminogen activator therapy in acute myocardial infarction. *J Am Coll Cardiol* 1991;17:467-73 [[1825097](#)]

Ray, 1993:

Ray SG, Pye M, Oldroyd KG, Christie J, Connelly DT, Northridge DB, Ford I, Morton JJ, Dargie HJ, Cobbe SM Early treatment with captopril after acute myocardial infarction. *Br Heart J* 1993;69:215-22 [[8461219](#)]

Sharpe, 1991:

Sharpe N, Smith H, Murphy J, Greaves S, Hart H, Gamble G Early prevention of left ventricular dysfunction after myocardial infarction with angiotensin-converting-enzyme inhibition. *Lancet* 1991;337:872-6 [[1672967](#)]

PRACTICAL (captopril), 1994:

Foy SG, Crozier IG, Turner JG, Richards AM, Frampton CM, Nicholls MG, Ikram H Comparison of enalapril versus captopril on left ventricular function and survival three months after acute myocardial infarction (the "PRACTICAL" study). *Am J Cardiol* 1994;73:1180-6 [[8203335](#)]

CONSENSUS 2, 1992:

Swedberg K, Held P, Kjekshus J, Rasmussen K, Ryden L, Wedel H Effects of the early administration of enalapril on mortality in patients with acute myocardial infarction. Results of the Cooperative New Scandinavian Enalapril Survival Study II (CONSENSUS II) *N Engl J Med* 1992 Sep 3;327:678-84 [[1495520](#)]

Schulman, 1995:

Schulman SP, Weiss JL, Becker LC, Guerci AD, Shapiro EP, Chandra NC, Siu C, Flaherty JT, Coombs V, Taube JC Effect of early enalapril therapy on left ventricular function and structure in acute myocardial infarction. *Am J Cardiol* 1995;76:764-70 [[7572651](#)]

FAMIS, 1998:

Borghesi C, Marino P, Zardini P, Magnani B, Collatina S, Ambrosioni E Short- and long-term effects of early foscipril administration in patients with acute anterior myocardial infarction undergoing intravenous thrombolysis: results from the Foscipril in Acute Myocardial Infarction Study. FAMIS Working Party. *Am Heart J* 1998;136:213-25 [[9704681](#)]

GISSI 3, 1994:

GISSI-3: effects of lisinopril and transdermal glyceryl trinitrate singly and together on 6-week mortality and ventricular function after acute myocardial infarction. Gruppo Italiano per lo Studio della Sopravvivenza nell'infarto Miocardico. *Lancet* 1994 May 7;343:1115-22 [[7910229](#)]

Wagner, 2002:

Wagner A, Herkner H, Schreiber W, Bur A, Woisetschlger C, Stix G, Laggner AN, Hirschl MM Ramipril prior to thrombolysis attenuates the early increase of PAI-1 in patients with acute myocardial infarction. *Thromb Haemost* 2002;88:180-5 [12195686]

SMILE, 1995:

Ambrosioni E, Borghi C, Magnani B The effect of the angiotensin-converting-enzyme inhibitor zofenopril on mortality and morbidity after anterior myocardial infarction. The Survival of Myocardial Infarction Long-Term Evaluation (SMILE) Study Investigators. *N Engl J Med* 1995 Jan 12;332:80-5 [7990904]

2 intravenous ACEI

Trial	Treatments	Patients	Trials design and methods
captopril vs placebo			
Bussmann , 1992 n=22/24 follow-up: 48h	slow intravenous bolus injection of 2.5 or 5.0 mg captopril followed by a continuous infusion of 1.5-2.0 mg/h for a period of 48 hours versus placebo	patients with acute myocardial infarction	Parallel groups double blind
CATS , 1996 n=149/149 follow-up: 1 year	captopril 25 mg three times a day versus placebo	patients with a first anterior myocardial infarction treated with intravenous streptokinase within 6h of onset of symptoms	Parallel groups double blind The Netherlands
CCS-1 , 1995 n=13634 follow-up: 1 month	captopril 6.25 mg initial dose, 12.5 mg 2 h later, and then 12.5 mg three times daily for 28 days versus placebo	Acute MI <36h of MI	Parallel groups double blind China
Di Pasquale , 1997 n=31/30 follow-up: 12h	captopril first dose 2-4 h after starting thrombolysis (the dose was then increased up to 25 mg every 8 h) versus placebo	patients hospitalized for suspected anterior AMI within 4 h from the onset of symptoms suitable for thrombolysis	Parallel groups double blind italy
Di Pasquale , 1994 n=188/183 follow-up: 2h	captopril, 6.25 mg, orally 15 min before thrombolysis versus placebo before thrombolysis	patients with acute myocardial infarction , hospitalized within 4 h of the onset of symptoms	Parallel groups double blind Italy
ECCE , 1997 n=104/104 follow-up: 1 month	captopril titrated dose in order to preserve their blood pressure versus placebo	patients with acute myocardial infarction	Parallel groups double blind
French , 1999 n=243/250 follow-up: 1 year	captopril 6.25 mg, increasing to 50 mg t.d.s. versus placebo	patients aged <or = 75 years with first infarctions, presenting within 4 h of symptom onset	Parallel groups double blind New Zealand
Galcera , 1993 n=21/22 follow-up: 14 days	captopril versus placebo	patients with a first acute myocardial infarction and a pulmonary capillary pressure equal or above 17 mmHg	Parallel groups double blind

continued...

Trial	Treatments	Patients	Trials design and methods
Hargreaves , 1992 n=36/36 follow-up: 28 days	12.5 mg of captopril three times daily versus placebo	patients with acute myocardial infarction (systolic blood pressure >90 mm Hg) within 24 hours of the start of pain	Parallel groups double blind UK
ISIS-4 , 1995 n=29028/29022 follow-up: 1 month	captopril 6.25mg twice daily initially titrated up to 50 mg twice daily (for 1 month) versus placebo	Acute MI <24h of MI, no cardiogenic shock or persistent severe hypotension	Factorial plan double blind 31 countries
Nabel , 1991 n=20/18 follow-up: 3 months	intravenous followed by oral captopril versus placebo	patients with myocardial infarction	Parallel groups double blind
Ray , 1993 n=99 follow-up: 1 year	captopril 25 mg three times a day versus placebo	haemodynamically stable patients with acute myocardial infarction, selected on clinical grounds as being at risk of late ventricular dilatation	Parallel groups double blind Glasgow
Sharpe , 1991 n=100 follow-up: 3 months	captopril 50 mg twice daily versus placebo	patients with Q wave myocardial infarction, but without clinical heart failure 24-48h after onset of symptoms	Parallel groups double blind
enalapril vs placebo			
CONSENSUS 2 , 1992 n=3044/3046 follow-up: 6 months	enalapril (1 mg IV infusion +5-20 mg PO daily) for 6 months versus placebo	patients with acute myocardial infarctions and blood pressure above 100/60 mm Hg, <24h of MI	Parallel groups double blind Scandinavia
Schulman , 1995 n=22/21 follow-up: 1 year	intravenous enalaprilat (1 mg) then oral treatment for 1 month versus placebo	patients with an acute Q-wave AMI within 24 hours of symptom onset	Parallel groups double blind US

References

Bussmann, 1992:

Bussmann WD, Micke G, Hildenbrand R, Klepzig H Jr [Captopril in acute myocardial infarct: its effect on infarct size and arrhythmias] Dtsch Med Wochenschr 1992;117:651-7 [1572248]

CATS, 1996:

van Gilst WH, Kingma JH, Peels KH, Dambrink JH, St John Sutton M Which patient benefits from early angiotensin-converting enzyme inhibition after myocardial infarction? Results of one-year serial echocardiographic follow-up from the Captopril and Thrombolysis Study (CATS). J Am Coll Cardiol 1996;28:114-21 [8752803]

CCS-1, 1995:

Oral captopril versus placebo among 13,634 patients with suspected acute myocardial infarction: interim report from the Chinese Cardiac Study (CCS-1) Lancet 1995 Mar 18;345:686-7 [7885123]

Di Pasquale, 1997:

Di Pasquale P, Bucca V, Scalzo S, Cannizzaro S, Longo AM, Alessi V, D'Amato M, Manusia F, Magatti MF [Is the reduction of the plasma levels of endothelin in the acute and sub-acute stage of myocardial infarct one of the beneficial effects of early treatment with ace inhibitors?] G Ital Cardiol 1996;26:673-80 [8803588]

Di Pasquale P, Valdes L, Albano V, Bucca V, Scalzo S, Pieri D, Maringhini G, Paterna S Early captopril treatment reduces plasma endothelin concentrations in the acute and subacute phases of myocardial infarction: a pilot study. J Cardiovasc Pharmacol 1997;29:202-8 [9057069]

Di Pasquale P, Bucca V, Scalzo S, Cannizzaro S, Longo AM, Alessi V, D'Amato M, Manusia F, Magatti MF [Is the reduction of the plasma levels of endothelin in the acute and sub-acute stage of myocardial infarct one of the beneficial effects of early treatment with ace inhibitors?] *G Ital Cardiol* 1996;26:673-80 [[8803588](#)]

Di Pasquale, 1994:

Di Pasquale P, Paterna S, Bucca V, Maringhini G, Magatti M Effects of the administration of captopril, metoprolol and of the captopril-metoprolol combination as adjuvant therapy during thrombolysis in acute myocardial infarction. *Int J Cardiol* 1994;46:107-12 [[7814158](#)]

Di Pasquale P, Paterna S, Cannizzaro S, Bucca V Does captopril treatment before thrombolysis in acute myocardial infarction attenuate reperfusion damage? Short-term and long-term effects. *Int J Cardiol* 1994;43:43-50 [[8175218](#)]

Di Pasquale P, Paterna S, Parrinello G, Bucca V, Cannizzaro S, Pipitone F, Maringhini G, Scalzo S, Licata G Captopril does not affect plasma endothelin-1 during thrombolysis and reperfusion. *Int J Cardiol* 1995;51:131-5 [[8522408](#)]

ECCE, 1997:

Kleber FX, Sabin GV, Winter UJ, Reindl I, Beil S, Wenzel M, Fischer M, Doering W Angiotensin-converting enzyme inhibitors in preventing remodeling and development of heart failure after acute myocardial infarction: results of the German multicenter study of the effects of captopril on cardiopulmonary exercise parameters (ECCE). *Am J Cardiol* 1997;80:162A-167A [[9293972](#)]

French, 1999:

French JK, Amos DJ, Williams BF, Cross DB, Elliott JM, Hart HH, Williams MG, Norris RM, Ashton NG, Whitlock RM, McLaughlin SC, White HD Effects of early captopril administration after thrombolysis on regional wall motion in relation to infarct artery blood flow. *J Am Coll Cardiol* 1999;33:139-45 [[9935020](#)]

Galcera, 1993:

Galcera-Tomas J, Nuo de la Rosa JA, Torres-Martinez G, Rodriguez-Garcia P, Castillo-Soria FJ, Canton-Martinez A, Campos-Peris JV, Pico-Aracil F, Ruiz-Ros JA, Ruiperez-Abizanda JA Effects of early use of captopril on haemodynamics and short-term ventricular remodelling in acute anterior myocardial infarction. *Eur Heart J* 1993;14:259-66 [[8449203](#)]

Hargreaves, 1992:

Hargreaves AD, Kolettis T, Jacob AJ, Flint LL, Turnbull LW, Muir AL, Boon NA Early vasodilator treatment in myocardial infarction: appropriate for the majority or minority? *Br Heart J* 1992;68:369-73 [[1449918](#)]

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 Mar 18;345:669-85 [[7661937](#)]

Nabel, 1991:

Nabel EG, Topol EJ, Galeana A, Ellis SG, Bates ER, Werns SW, Walton JA, Muller DW, Schwaiger M, Pitt B A randomized placebo-controlled trial of combined early intravenous captopril and recombinant tissue-type plasminogen activator therapy in acute myocardial infarction. *J Am Coll Cardiol* 1991;17:467-73 [[1825097](#)]

Ray, 1993:

Ray SG, Pye M, Oldroyd KG, Christie J, Connelly DT, Northridge DB, Ford I, Morton JJ, Dargie HJ, Cobbe SM Early treatment with captopril after acute myocardial infarction. *Br Heart J* 1993;69:215-22 [[8461219](#)]

Sharpe, 1991:

Sharpe N, Smith H, Murphy J, Greaves S, Hart H, Gamble G Early prevention of left ventricular dysfunction after myocardial infarction with angiotensin-converting-enzyme inhibition. *Lancet* 1991;337:872-6 [[1672967](#)]

CONSENSUS 2, 1992:

Swedberg K, Held P, Kjekshus J, Rasmussen K, Ryden L, Wedel H Effects of the early administration of enalapril on mortality in patients with acute myocardial infarction. Results of the Cooperative New Scandinavian Enalapril Survival Study II (CONSENSUS II) *N Engl J Med* 1992 Sep 3;327:678-84 [[1495520](#)]

Schulman, 1995:

Schulman SP, Weiss JL, Becker LC, Guerci AD, Shapiro EP, Chandra NC, Siu C, Flaherty JT, Coombs V, Taube JC Effect of early enalapril therapy on left ventricular function and structure in acute myocardial infarction. *Am J Cardiol* 1995;76:764-70 [[7572651](#)]

3 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.