Clinical trials of ramipril

TrialResults-center www.trialresultscenter.org

1 acute myocardial infarction

Trial	Treatments	Patients	Trials design and methods
ramipril vs placebo			
AIRE , 1993 n=1004/992 follow-up: 1.25 y	Ramipril 25 mg twice daily initial dose, up to 5 mg twice daily for at least 6 months versus placebo	patient within 310 days of a MI,with clinical evidence of heart failure	Parallel groups Double blind 14 countries
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

More details and results :

- 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

References

AIRE, 1993:

Effect of ramipril on mortality and morbidity of survivors of acute myocardial infarction with clinical evidence of heart failure. The Acute Infarction Ramipril Efficacy (AIRE) Study Investigators. Lancet 1993 Oct 2;342:821-8 [8104270]

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]

2 hypertension

Trial	Treatments	Patients	Trials design and methods
ramipril vs usual care			
Li et al , 2003 n=30/30 follow-up: 12 months	Ramipril 5 mg/day versus Conventional treatment	patients with end-stage renal failure treated with peritoneal dialysis	open
ramipril vs amlodipine			
AASK (ramipril vs amlodipine) , 2002 n=436/217 follow-up: 30 y	ramipril 2.5-10 mg/d versus amlodipine 5-10 mg/d	African Americans aged 18 to 70 years with hypertensive renal disease (GFR, 20-65 mL/min per 1.73 m(2))	Parallel groups Double blind US
ramipril vs metoprolol			
AASK (ramipril vs metoprolol) , 2002 n=436/441 follow-up: 41 y	ramipril 2.5-10 mg/d versus metoprolol 50-200 mg/d	African Americans aged 18 to 70 years with hypertensive renal disease (GFR, 20-65 mL/min per 1.73 m(2))	Parallel groups Double blind US
Telmisartan + ramipril vs Ramipril			
ONTARGET/Tel+Ram , 2008 n=8502/8576 follow-up: 4.7 y	Telmisartan + ramipril versus Ramipril	patients with vascular disease or high-risk diabetes	Parallel groups double-blind

More details and results :

- anti hypertensive agents for hypertension in all type of patient at http://www.trialresultscenter.org/go-Q13
- anti hypertensive agents for hypertension in nephropathy at http://www.trialresultscenter.org/go-Q19
- 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

References

Li et al, 2003:

Li PK, Chow KM, Wong TY, Leung CB, Szeto CC Ann Intern Med 2003;139:105-12 [12859160]

AASK (ramipril vs amlodipine), 2002:

Wright JT Jr, Bakris G, Greene T, Agodoa LY, Appel LJ, Charleston J, Cheek D, Douglas-Baltimore JG, Gassman J, Glassock R, Hebert L, Jamerson K, Lewis J, Phillips RA, Toto RD, Middleton JP, Rostand SG Effect of blood pressure lowering and antihypertensive drug class on progression of hypertensive kidney disease: results from the AASK trial. JAMA 2002;288:2421-31 [12435255]

AASK (ramipril vs metoprolol), 2002:

Wright JT Jr, Bakris G, Greene T, Agodoa LY, Appel LJ, Charleston J, Cheek D, Douglas-Baltimore JG, Gassman J, Glassock R, Hebert L, Jamerson K, Lewis J, Phillips RA, Toto RD, Middleton JP, Rostand SG Effect of blood pressure lowering and antihypertensive drug class on progression of hypertensive kidney disease: results from the AASK trial. JAMA 2002;288:2421-31 [12435255]

Norris K, Bourgoigne J, Gassman J, Hebert L, Middleton J, Phillips RA, Randall O, Rostand S, Sherer S, Toto RD, Wright JT Jr, Wang X, Greene T, Appel LJ, Lewis J Cardiovascular outcomes in the African American Study of Kidney Disease and Hypertension (AASK) Trial. Am J Kidney Dis 2006;48:739-51 [17059993] 10.1053/j.ajkd.2006.08.004

ONTARGET/Tel+Ram, 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;358:1547-59 [18378520]

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]

3 heart failure

Trial	Treatments	Patients	Trials design and methods
ramipril vs control			
Swedberg , 1991 n=115/108 follow-up:	-	-	
ramipril vs placebo			
AIRE , 1993 n=1004/992 follow-up: 1.25 y	Ramipril 25 mg twice daily initial dose, up to 5 mg twice daily for at least 6 months versus placebo	patient within 310 days of a MI,with clinical evidence of heart failure	Parallel groups Double blind 14 countries
Gordon , 1991 *unpublished* n=94/98 follow-up: 12 weeks	ramipril 10mg/d versus placebo	patients with herat failure and LVFE<=35%	Parallel groups double blind USA

continued...

Trial	Treatments	Patients	Trials design and methods
Gundersen , 1994 n=104/91 follow-up: 12 weeks	ramipril titrated from 1.25 mg to a maximum of 10 mg once daily versus placebo	patients with NYHA II-III CHF, LVFE<=40% and size of the heart >600ml/m2 for mean or >550ml/m2 for women	Parallel groups double blind four Nordic countries
Lemarie , 1992 *unpublished* n=42/43 follow-up: 24 weeks	ramipril 2.5mg twice daily versus placebo	patient with NYHA II-III heart failure	Parallel groups double blind France
Maass-a , 1991 *unpublished* n=87/45 follow-up:	ramipril versus placebo	patients with heart failure	
Maass-b , 1991 *unpublished* n=329/171 follow-up: 12 weeks	ramirpil 5 or 10 mg once daily versus placebo	patient with NYHA II-III heart failure and LVFE<=40%	Parallel groups double blind Europe
Maass-c , 1991 *unpublished* n=47/48 follow-up: 12 weeks	ramipril 10mg once daily versus placebo	patient with heart failure with LVFE<=35%	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
- angiotensin-Converting Enzyme Inhibitors for heart failure in MI patients with LV dysfunction without clinical evidence of HF at http://www.trialresultscenter.org/go-Q238

References

Swedberg, 1991:

Swedberg K, Amtorp 0, 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

AIRE, 1993:

Effect of ramipril on mortality and morbidity of survivors of acute myocardial infarction with clinical evidence of heart failure. The Acute Infarction Ramipril Efficacy (AIRE) Study Investigators. Lancet 1993 Oct 2;342:821-8 [8104270]

Gordon, 1991:

unpublished

Gordon M Evaluation of the Efficacy and Safety of Ramipril (HOE 498) in Patients With Congestive Heart Failure in a Placebo-Controlled Trial. Somerville, NJ: Hoechst-Roussel Pharmaceuticals; October 1991. Unpublished report

Lubsen J, Chadha DR, Yotof YT, Swedberg K Meta-analysis of morbidity and mortality in five exercise capacity trials evaluating ramipril in chronic congestive cardiac failure. Am J Cardiol 1996 Jun 1;77:1191-6 [8651094]

Gundersen, 1994:

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Lemarie, 1992:

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Lemarie JC. Multicenter Double-Blind Placebo Controlled Study of the Efficacy and Safety of Ramipril Administered Orally for 24 Weeks in the Treatment of Stable Chronic Congestive Cardiac Failure. Paris, France: Laboratories Hoechst; December 1992. Unpublished report

Lubsen J, Chadha DR, Yotof YT, Swedberg K Meta-analysis of morbidity and mortality in five exercise capacity trials evaluating ramipril in chronic congestive cardiac failure. Am J Cardiol 1996 Jun 1;77:1191-6 [8651094]

Maass-a, 1991:

unpublished

Maass L Double-Blind Comparative Trial With Ramipril and Placebo in Patients With Heart Failure (NYHA Class 1I1-IV) Stabilized on Digitalis and Furosemides Frankfurt, Germany: Hoechst Aktiengesellschaft; October 1991. Unpublished report

Maass-b, 1991:

unpublished

Maass L Efficacy and Safety ofRamipril (HOE498) in Patients With Congestive Heart Failure in a Double Blind Placebo Controlled Trial Frankfurt, Germany: Hoechst Aktiengesellschaft; October 1991. Unpublished report

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Maass L. Evaluation of the Effect of Ramipril (HOE 498) on Exercise Duration, Invasive Cardiac Hemodynamics Profiles, and Safety in Patients With Congestive Heart Failure. Frankfurt, Germany: Hoechst Aktiengesellschaft; October 1991. Unpublished report.

Lubsen J, Chadha DR, Yotof YT, Swedberg K Meta-analysis of morbidity and mortality in five exercise capacity trials evaluating ramipril in chronic congestive cardiac failure. Am J Cardiol 1996 Jun 1;77:1191-6 [8651094]

4 miscellaneous

Trial	Treatments	Patients	Trials design and methods
telmisartan + ramipril vs ramipril			
ONTARGET (association vs ramipril) , 2008 [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

continued...

Trial	Treatments	Patients	Trials design and methods
telmisartan + ramipril vs telmisartan			
ONTARGET (association vs telmisartan) , 2008 [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

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]

5 atrial fibrillation

Trial	Treatments	Patients	Trials design and methods
ramipril vs placebo			
Brown *ongoing* [NCT00141778] n=777 follow-up:	ramipril or spironolactone versus placebo	AF following CPB surgery	

More details and results :

- prevention for atrial fibrillation in patient with history of atrial fibrillation at http://www.trialresultscenter.org/go-Q328

References

Brown, :

ongoing trial NCT00141778

6 diabetes type 2

Trial	Treatments	Patients	Trials design and methods
ramipril vs placebo			
DREAM ramipril , 2006 [NCT00095654] n=2623/2646 follow-up: 3 y (median)	ramipril up to 15 mg daily versus placebo	patients with impaired fasting glucose or impaired glucose tolerance, or both, and no previous cardiovascular disease	Parallel groups double blind 21 countries
DIABHYCAR , 2004 n=2443/2469 follow-up: median 4 years	ramipril 1.25 mg/day versus placebo	patients with type 2 diabetes who have microalbuminuria or proteinuria	Parallel groups double-blind Europe, North Africa
DREAM , 2008 n=2623/2646 follow-up: 3 years	ramipril(up to 15 mg per day) versus placebo	people aged >=30 years, with Impaired glucose tolerance and/or impaired fasting glucose without known CVD or renal insufficiency	Factorial plan open

More details and results :

- prevention for diabetes type 2 in all type of patients at http://www.trialresultscenter.org/go-Q341
- 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

References

DREAM ramipril, 2006:

Gerstein HC, Yusuf S, Bosch J, Pogue J, Sheridan P, Dinccag N, Hanefeld M, Hoogwerf B, Laakso M, Mohan V, Shaw J, Zinman B, Holman RR Lancet 2006 Sep 23;368:1096-105 [16997664]

Bosch J, Yusuf S, Gerstein HC, Pogue J, Sheridan P, Dagenais G, Diaz R, Avezum A, Lanas F, Probstfield J, Fodor G, Holman RR Effect of ramipril on the incidence of diabetes. N Engl J Med 2006;355:1551-62 [16980380]

DIABHYCAR, 2004:

Marre M, Lievre M, Chatellier G, Mann JF, Passa P, Mnard J Effects of low dose ramipril on cardiovascular and renal outcomes in patients with type 2 diabetes and raised excretion of urinary albumin: randomised, double blind, placebo controlled trial (the DIABHYCAR study). BMJ 2004;328:495 [14960504] 10.1136/bmj.37970.629537.0D

DREAM, 2008:

Dagenais GR, Gerstein HC, Holman R, Budaj A, Escalante A, Hedner T, Keltai M, Lonn E, McFarlane S, McQueen M, Teo K, Sheridan P, Bosch J, Pogue J, Yusuf S Effects of ramipril and rosiglitazone on cardiovascular and renal outcomes in people with impaired glucose tolerance or impaired fasting glucose: results of the Diabetes REduction Assessment with ramipril and rosiglitazone Medication (DREAM) trial. Diabetes Care 2008;31:1007-14 [18268075] 10.2337/dc07-1868

Bosch J, Yusuf S, Gerstein HC, Pogue J, Sheridan P, Dagenais G, Diaz R, Avezum A, Lanas F, Probstfield J, Fodor G, Holman RR Effect of ramipril on the incidence of diabetes. N Engl J Med 2006;355:1551-62 [16980380] 10.1056/NEJMoa065061

7 patients at high risk for cardiovascular events

Trial	Treatments	Patients	Trials design and methods
ramipril vs placebo			
HOPE , 2000 n=4645/4652 follow-up: 5 y	ramipril 10 mg once per day orally versus placebo	high-risk patients (55 years of age or older) with evidence of vascular disease or diabetes plus one other cardiovascular risk factor and who were not known to have a low ejection fraction or heart failure	Parallel groups double blind
telmisartan + ramipril vs ramipril			
ONTARGET (association vs ramipril) , 2008 [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
telmisartan + ramipril vs telmisartan			
ONTARGET (association vs telmisartan) , 2008 [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 patients at high risk for cardiovascular events in all type of patients at http://www.trialresultscenter.org/go-Q97
- angiotensin-Converting Enzyme Inhibitors for patients at high risk for cardiovascular events in all type of patients at http://www.trialresultscenter.org/go-Q98
- inhibition of the renin-angiotensin system (ACEI or ARB) for patients at high risk for cardiovascular events in all type of patients at http://www.trialresultscenter.org/go-Q157

References

HOPE, 2000:

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]

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 Jan 20;342:145-53 [10639539]

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]

8 impaired fasting glucose

Trial	Treatments	Patients	Trials design and methods
ramipril vs placebo			
DREAM ramipril , 2006 [NCT00095654] n=2623/2646 follow-up: 3 y (median)	ramipril up to 15 mg daily versus placebo	patients with impaired fasting glucose or impaired glucose tolerance, or both, and no previous cardiovascular disease	Parallel groups double blind 21 countries

More details and results :

- prevention for impaired fasting glucose in all type of patients at http://www.trialresultscenter.org/go-Q342

References

DREAM ramipril, 2006:

Gerstein HC, Yusuf S, Bosch J, Pogue J, Sheridan P, Dinccag N, Hanefeld M, Hoogwerf B, Laakso M, Mohan V, Shaw J, Zinman B, Holman RR Lancet 2006 Sep 23;368:1096-105 [16997664]

Bosch J, Yusuf S, Gerstein HC, Pogue J, Sheridan P, Dagenais G, Diaz R, Avezum A, Lanas F, Probstfield J, Fodor G, Holman RR Effect of ramipril on the incidence of diabetes. N Engl J Med 2006;355:1551-62 [16980380]

9 diabetic kidney disease

Trial	Treatments	Patients	Trials design and methods
ramipril vs placebo			
DIABHYCAR , 2004 n=2443/2469 follow-up: median 4 years	ramipril 1.25 mg/day versus placebo	patients with type 2 diabetes who have microalbuminuria or proteinuria	Parallel groups double-blind Europe, North Africa

More details and results :

- All mechanism for diabetic kidney disease in all type of patients at http://www.trialresultscenter.org/go-Q667

References

DIABHYCAR, 2004:

Marre M, Lievre M, Chatellier G, Mann JF, Passa P, Mnard J Effects of low dose ramipril on cardiovascular and renal outcomes in patients with type 2 diabetes and raised excretion of urinary albumin: randomised, double blind, placebo controlled trial (the DIABHYCAR study). BMJ 2004;328:495 [14960504] 10.1136/bmj.37970.629537.0D

Entry terms: Triatec, Altace, Delix, Ramace, Vesdil, Carasel, Acovil, Tritace, Zabien