Clinical trials of ACE inhibitor

TrialResults-center www.trialresultscenter.org

1 acute myocardial infarction

Trial	Treatments	Patients	Trials design and methods
Valsartan+ACE inhibitor vs ACE inhibitor only			
VALIANT (valsartan+capropril) , 2003 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

More details and results :

- angiotensin-receptor blockers for acute myocardial infarction in all type of patients at http://www.trialresultscenter.org/go-Q253

References

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]

2 hypertension

Trial	Treatments	Patients	Trials design and methods
ACE inhibitors vs placebo			
HOPE (diabetic subgroup) , 2000 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
ACE inhibitor vs calcium-channel blocker			

continued...

Trial	Treatments	Patients	Trials design and methods
STOP-2 (ACEI vs CCB) (diabetic subgroup) , 2000 n=235/231 follow-up: 5.03y	ACE inhibitor versus calcium antagonists	diabetic (subgroup) elderly patients aged 70-84 years	open with blind assessment Sweden
ACE inhibitor vs diuretic or beta-blocker			
STOP-2 (ACEI, diabetic subgroup) , 2000 n=235/253 follow-up: 5.03y	ACE inhibitor versus conventional treatment (diuretic or beta-blocker)	diabetic (subgroup) elderly patients aged 70-84 years with hypertension	Parallel groups open with blind assessment Sweden

More details and results :

- anti hypertensive agents for hypertension in diabetic patients at http://www.trialresultscenter.org/go-Q10

References

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]

STOP-2 (ACEI vs CCB) (diabetic subgroup), 2000:

Lindholm LH, Hansson L, Ekbom T, Dahlf B, Lanke J, Linjer E, Scherstn B, Wester PO, Hedner T, de Faire U Comparison of antihypertensive treatments in preventing cardiovascular events in elderly diabetic patients: results from the Swedish Trial in Old Patients with Hypertension-2. STOP Hypertension-2 Study Group. J Hypertens 2000 Nov;18:1671-5 [11081782]

Hansson L, Lindholm LH, Ekbom T, Dahlf B, Lanke J, Scherstn B, Wester PO, Hedner T, de Faire U Randomised trial of old and new antihypertensive drugs in elderly patients: cardiovascular mortality and morbidity the Swedish Trial in Old Patients with Hypertension-2 study. Lancet 1999;354:1751-6 [10577635]

STOP-2 (ACEI, diabetic subgroup), 2000:

Lindholm LH, Hansson L, Ekbom T, Dahlf B, Lanke J, Linjer E, Scherstn B, Wester PO, Hedner T, de Faire U Comparison of antihypertensive treatments in preventing cardiovascular events in elderly diabetic patients: results from the Swedish Trial in Old Patients with Hypertension-2. STOP Hypertension-2 Study Group. J Hypertens 2000;18:1671-5 [11081782]

Hansson L, Lindholm LH, Ekbom T, Dahlf B, Lanke J, Scherstn B, Wester PO, Hedner T, de Faire U Randomised trial of old and new antihypertensive drugs in elderly patients: cardiovascular mortality and morbidity the Swedish Trial in Old Patients with Hypertension-2 study. Lancet 1999;354:1751-6 [10577635]

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3 heart failure

Trial	Treatments	Patients	Trials design and methods
candesartan+ACE inhibitor vs ACE inhibitor only			
RESOLVD association , 1999 n=332/109 follow-up: 43 wk	Candesartan, 4 mg, 8mg daily, plus enalapril, 10 mg twice daily versus Enalapril, 10 mg twice daily	Patients with New York Heart Association functional class NYHA II, III, or IV CHF, 6-minute walk distance (6MWD) >500 m, and ejection fraction (EF) <0.40	Parallel groups multicenter
CHARM-Added , 2003 n=1276/1272 follow-up: Median, 41 mo	Candesartantarget dose 32 mg once daily versus Placebo	patients with New York Heart Association functional class IIIV CHF and left-ventricular ejection fraction40% or lower, and who were being treated with ACE inhibitors.	Parallel groups double blind 26 countries
eprosartan+ACE inhibitor vs ACE inhibitor only			
ADEPT , 2001 n=18/18 follow-up: 8 wk	Eprosartan, 400 to 800 mg twice daily versus Placebo	patients with stable New York Heart Association class II-IV CHF receiving ACE inhibitor therapy	Parallel groups double blind
irbesartan+ACE inhibitor vs ACE inhibitor only			
Tonkon et al. , 2000 n=57/52 follow-up: 12 wk	Irbesartan, 150 mg daily (plus ACE inhibitor) versus Placebo (plus ACE inhibitor)	patients with heart failure (New York Heart Association functional class II and III) and left ventricular ejection fraction (LVEF) <or = 40% received stable doses of ACE inhibitors and diuretics	Parallel groups double blind
losartan+ACE inhibitor vs ACE inhibitor only			
Hamroff et al. , 1999 n=16/17 follow-up: 6 mo	Losartan, 50 mg daily (plus ACE inhibitor) versus Placebo (plus ACE inhibitor)	patients with severe congestive heart failure (NYHA III-IV) despite treatment with maximally recommended or tolerated doses of ACE inhibitors	Parallel groups double blind
valsartan+ACE inhibitor vs ACE inhibitor only			
V-HeFT , 1999 n=55/28 follow-up: 4 wk	Valsartan 80 mg and 160mg twice daily (plus ACE inhibitor) versus Placebo (plus usual ACE inhibitor)	Patients with stable symptomatic congestive heart failure (CHF) receiving long-term ACE inhibitor therapy (NYHA functional class II,III, or IV) and PCWP >or=to 15 mm Hg	Parallel groups Double blind US
Val-HeFT , 2001 n=2511/2499 follow-up: 23 mo	Valsartan, 160 mg twice daily (plus ACE inhibitor) versus Placebo (plus ACE inhibitor)	patients with heart failure of New York Heart Association (NYHA) class II, III, or IV	Parallel groups Double blind 16 countries

More details and results :

- 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 already receiving ACE inhibitor at http://www.trialresultscenter.org/go-Q68

References

RESOLVD association, 1999:

McKelvie RS, Yusuf S, Pericak D, Avezum A, Burns RJ, Probstfield J, Tsuyuki RT, White M, Rouleau J, Latini R, Maggioni A, Young J, Pogue J Comparison of candesartan, enalapril, and their combination in congestive heart failure: randomized evaluation of strategies for left ventricular dysfunction (RESOLVD) pilot study. The RESOLVD Pilot Study Investigators. Circulation 1999 Sep 7;100:1056-64 [10477530]

CHARM-Added, 2003:

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 Sep 6;362:767-71 [13678869]

Weir RA, McMurray JJ, Puu M, Solomon SD, Olofsson B, Granger CB, Yusuf S, Michelson EL, Swedberg K, Pfeffer MA, , Efficacy and tolerability of adding an angiotensin receptor blocker in patients with heart failure already receiving an angiotensin-converting inhibitor plus aldosterone antagonist, with or without a beta blocker. Findings from the Candesartan in Heart failure: Assessment of Reduction in Mortality and morbidity (CHARM)-Added trial. Eur J Heart Fail 2008;10:157-63. [18242128] 10.1016/j.ejheart.2007.12.006

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Murdoch DR, McDonagh TA, Farmer R, Morton JJ, McMurray JJ, Dargie HJ ADEPT: Addition of the AT1 receptor antagonist eprosartan to ACE inhibitor therapy in chronic heart failure trial: hemodynamic and neurohormonal effects. Am Heart J 2001 May;141:800-7 [11320369]

Tonkon et al., 2000:

Tonkon M, Awan N, Niazi I, Hanley P, Baruch L, Wolf RA, Block AJ A study of the efficacy and safety of irbesartan in combination with conventional therapy, including ACE inhibitors, in heart failure. Irbesartan Heart Failure Group. Int J Clin Pract 2000 Jan-Feb;54:11-4, 16-8 [10750252]

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Hamroff G, Katz SD, Mancini D, Blaufarb I, Bijou R, Patel R, Jondeau G, Olivari MT, Thomas S, Le Jemtel TH Addition of angiotensin II receptor blockade to maximal angiotensin-converting enzyme inhibition improves exercise capacity in patients with severe congestive heart failure. Circulation 1999 Mar 2;99:990-2 [10051289]

V-HeFT, 1999:

Baruch L, Anand I, Cohen IS, Ziesche S, Judd D, Cohn JN Augmented short- and long-term hemodynamic and hormonal effects of an angiotensin receptor blocker added to angiotensin converting enzyme inhibitor therapy in patients with heart failure. Vasodilator Heart Failure Trial (V-HeFT) Study Group. Circulation 1999 May 25;99:2658-64 [10338459]

Val-HeFT, 2001:

Cohn JN, Tognoni G A randomized trial of the angiotensin-receptor blocker valsartan in chronic heart failure. N Engl J Med 2001 Dec 6;345:1667-75 [11759645]

4 diabetes type 2

Trial	Treatments	Patients	Trials design and methods
ACE inhibitors vs placebo			
HOPE (diabetic subgroup) , 2000 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
ACE inhibitor vs calcium-channel blocker			
STOP-2 (ACEI vs CCB) (diabetic subgroup) , 2000 n=235/231 follow-up: 5.03y	ACE inhibitor versus calcium antagonists	diabetic (subgroup) elderly patients aged 70-84 years	open with blind assessment Sweden
ACE inhibitor vs diuretic or beta-blocker			
STOP-2 (ACEI, diabetic subgroup) , 2000 n=235/253 follow-up: 5.03y	ACE inhibitor versus conventional treatment (diuretic or beta-blocker)	diabetic (subgroup) elderly patients aged 70-84 years with hypertension	Parallel groups open with blind assessment Sweden

More details and results :

- anti hypertensive agents for diabetes type 2 in patients with hypertension at http://www.trialresultscenter.org/go-Q83
- anti hypertensive agents for diabetes type 2 in patients with or without hypertension at http://www.trialresultscenter.org/go-Q414
- angiotensin renin system blockade for diabetes type 2 in all type of patients at http://www.trialresultscenter.org/go-Q438

References

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]

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Hansson L, Hedner T, Dahlf B Prospective randomized open blinded end-point (PROBE) study. A novel design for intervention trials. Prospective Randomized Open Blinded End-Point. Blood Press 1992;1:113-9 [1366259]

Entry terms: candesartan, candesartan cilexetil, 1-(cyclohexylocarbonyloxy)ethyl-2-ethoxy-1-(2'-(1H-tetrazol-5-yl)biphenyl-4-yl)-1H-benzimidazole-7-carboxylate, TCV 116, TCV-116, Atacand, Astra brand of candesartan cilexetil, Takeda brand of candesartan cilexetil, Blopress, Kenzen, Promed brand of candesartan cilexetil, Amias, AstraZeneca brand of candesartan cilexetil, Parapres, Almirall brand of candesartan cilexetil, , candesartan, 2-ethoxy-7-carboxy-1-(2'-(1H-tetrazol-5-yl)biphenyl-4-yl)methylbenzimidazole, CV 11974, CV11974, CV-11974, , irbesartan, Aprovel, Avapro, Karvea, losartan, Losartan, Cozaar, MK-954, MK 954, MK954, DuP-753, DuP 753, DuP753, Losartan Potassium, Losartan Monopotassium Salt, , valsartan, valsartan, N-valeryl-N-((2'-(1H-tetrazol-5-yl)biphenyl-4-yl)methyl)valine, Diovan, Tareg, Novartis brand of valsartan, Kalpress, Lacer brand of valsartan, Miten, CEPA brand of valsartan, Provas, Schwarz brand of valsartan, Sanol brand of valsartan, Vals, Esteve brand of valsartan, walsartan, CGP 48933, Nisis, Aventis brand of valsartan,