Clinical trials of angiotensin-receptor blockers for heart failure in patients already receiving ACE inhibitor

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1 angiotensin receptor blocker

Trial	Treatments	Patients	Trials design and methods
losartan vs enalapril			
Dickstein et al. , 1995 n=108/58 follow-up: 8 wk	Losartan, 25 mg, 50mg daily versus Enalapril, 10 mg twice daily	patients with moderate or severe chronic heart failure in New York Heart Association functional class III or IV and an ejection fraction <or = 35%	Parallel groups double blind
Lang et al. , 1997 n=78/38 follow-up: 12 wk	Losartan titrated to 25 mg ou 50 mg daily versus Enalapril, titrated to 10 mg twice daily	patients with congestive heart failure (New York Heart Association functionalclasses II to IV) and left ventricular ejection fraction <= 45% previously treated with stable doses of ACE inhibitors and diureticagents, with or without concurrent digitalis and othervasodilators	Parallel groups Double blind US, Canada
telmisartan vs enalapril			
REPLACE , 2001 n=301/77 follow-up: 12 wk	Telmisartan, 10 mg, 20mg, 40mg, 80mg daily versus Enalapril, 10 mg twice daily	ambulatory patients at least 21 years of age, in sinus rhythm, with chronic moderatesymptomatic heart failure (New York Heart Associatality.tion class IIIII) and a left ventricular ejection fraction of 40% or lower	Parallel groups Double blind
valsartan vs enalapril			
HEAVEN , 2002 n=70/71 follow-up: 12 wk	Valsartan, 160 mg daily versus Enalapril, 10 mg twice daily	Men and women with mild/moderate heart failure stabilised on an angiotensin-converting enzyme inhibitor and left ventricular ejection fraction 0.45 or less	Parallel groups Double blind

References

Dickstein et al., 1995:

Dickstein K, Chang P, Willenheimer R, Haunso S, Remes J, Hall C, Kjekshus J Comparison of the effects of losartan and enalapril on clinical status and exercise performance in patients with moderate or severe chronic heart failure. J Am Coll Cardiol 1995 Aug;26:438-45 [7608448]

Lang et al., 1997:

Lang RM, Elkayam U, Yellen LG, Krauss D, McKelvie RS, Vaughan DE, Ney DE, Makris L, Chang PI Comparative effects of losartan and enalapril on exercise capacity and clinical status in patients with heart failure. The Losartan Pilot Exercise Study Investigators. J Am Coll Cardiol 1997 Oct;30:983-91 [9316528]

REPLACE, 2001:

Dunselman PH Effects of the replacement of the angiotensin converting enzyme inhibitor enalapril by the angiotensin II receptor blocker telmisartan in patients with congestive

heart failure. The replacement of angiotensin converting enzyme inhibition (REPLACE) investigators. Int J Cardiol 2001 Feb;77:131-8; discussion 139-40 [11182175]

HEAVEN, 2002:

Willenheimer R, Helmers C, Pantev E, Rydberg E, Lofdahl P, Gordon A Safety and efficacy of valsartan versus enalapril in heart failure patients. Int J Cardiol 2002 Oct;85:261-70 [12208593]

2 ARBs added to ACEI

Trial	Treatments	Patients	Trials design and methods
candesartan+ACE inhibitor vs ACE inhibitor only			
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

References

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

ADEPT, 2001:

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]

Hamroff et al., 1999:

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]

3 About TrialResults-center.org

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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.

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