

Clinical trials of aldosterone blockade for heart failure in all type of patients

TrialResults-center www.trialresultscenter.org

1 aldosterone-receptor blockers

Trial	Treatments	Patients	Trials design and methods
spironolactone vs control			
Cicoira , 2002 n=54/52 follow-up: 12 months	spironolactone 12.5 to 50 mg/day versus control	patients with chronic heart failure	Parallel groups open
Cicoira , 2004 n=47/46 follow-up: 12 months	spironolactone versus control	chronic heart failure patients	open
Ramires , 2000 n=19/16 follow-up: 20 weeks	spironolactone versus standard medical treatment	patients with systolic dysfunction and NYHA class III CHF secondary to dilated or ischemic cardiomyopathy	Parallel groups open
eplerenone vs placebo			
EMPHASIS-HF , 2010 [NCT00232180] n=1364/1373 follow-up: 21 months	eplerenone versus placebo	patients with New York Heart Association class II heart failure and an ejection fraction of no more than 35%	Parallel groups double blind 29 countries
EPHESUS , 2003 n=3319/3313 follow-up: 16 mo (mean, range 0 to 33)	eplerenone 25 mg per day initially, titrated to a maximum of 50 mg per day versus placebo	patients with acute myocardial infarction complicated by left ventricular dysfunction and heart failure	Parallel groups Double blind 37 countries
REMODEL <i>ongoing</i> [NCT00082589] n=NA follow-up:	Eplerenone versus placebo	Patients with left ventricular systolic dysfunction (EF Less Than or Equal to 35%) and mild to moderate heart failure	Parallel groups double blind
Weir <i>ongoing</i> [NCT00132093] n=NA follow-up: 6 monthsh	eplerenone versus placebo	patients with acute myocardial infarction	Parallel groups double blind
spironolactone vs placebo			
Agostoni , 2005 n=14/15 follow-up: 6 months	spironolactone 25mg/d versus placebo	stable chronic heart failure patients with reduced influences lung diffusion (DLCO)	Parallel groups open Italy
Farquharson , 2000 n=10/10 follow-up: 4 weeks	spironolactone 50 mg/d versus placebo	patients with NYHA class II to III chronic heart failure on standard diuretic/ACE inhibitor therapy	double blind

continued...

Trial	Treatments	Patients	Trials design and methods
Macdonald , 2004 n=43/43 follow-up: 3 months	spironolactone 12.5-50 mg/d versus placebo	patients with New York Heart Association class I-II congestive heart failure taking optimal treatment (including beta blockers)	Cross over double blind
MacFadyen , 1997 n=21/16 follow-up: 8 weeks	spironolactone (50-100 mg/day) versus placebo	patients with stable chronic heart failure	Parallel groups double blind
Mottram , 2004 n=30 follow-up: 6 months	spironolactone 25 mg/d versus placebo	hypertensive patients with diastolic heart failure	double blind
RALES , 1998 n=822/841 follow-up: 24 mo	spironolactone (25 to 50 mg daily) versus placebo	patients with severe heart failure	Parallel groups Open World
Tsutamoto , 2001 n=20/17 follow-up: 12 weeks	spironolactone 25 mg daily versus placebo	patients with mild-to-moderate nonischemic congestive heart failure	Parallel groups double blind Japan
Yee , 2001 n=28/28 follow-up: 4 weeks	spironolactone 50mg/d versus placebo	patients with New York Heart Association class II to IV congestive heart failure	double blind
PIE II ongoing [NCT00123955] n=NA follow-up: 9 months	Spironolactone 25mg tablet daily for 9 months versus placebo	elderly patients with isolated diastolic heart failure	Parallel groups double blind
spironolactone+captopril vs captopril			
Han , 1994 n=19/16 follow-up: 4 weeks	captopril plus spironolactone versus captopril alone	patients with refractory CHF and New York Heart Association functional class IV without renal dysfunction, hypotension and hyperkalemia	open China
aldactone vs furosemide			
Bednarz , 2000 n=11/10 follow-up:	Aldactone 200 mg i.v versus furosemide 20 mg i.v	patients with NYHA class III to IV congestive heart failure	open
spironolactone vs spironolactone			
Nouvel essai ongoing [NCT00125437] n=NA follow-up:	spironolactone larger dose versus spironolactone standard dose	severe congestive heart failure in patients with nonischemic cardiomyopathy	Parallel groups single blind
spironolactone+furosemide vs spironolactone+butizide			
Mauersberger , 1985 n=22 follow-up:	spironolactone 50mg + furosemide 20 mg versus spironolactone 50mg + butizide 5mg	patients with congestive heart failure	open

References

Cicoira, 2002:

Cicoira M, Zanolla L, Rossi A, Golia G, Franceschini L, Brighetti G, Marino P, Zardini P, Long-term, dose-dependent effects of spironolactone on left ventricular function and exercise tolerance in patients with chronic heart failure. *J Am Coll Cardiol* 2002;40:304-10. [[12106936](#)]

Cicoira, 2004:

Cicoira M, Rossi A, Bonapace S, Zanolla L, Perrot A, Francis DP, Golia G, Franceschini L, Osterziel KJ, Zardini P, Effects of ACE gene insertion/deletion polymorphism on response to spironolactone in patients with chronic heart failure. *Am J Med* 2004;116:657-61. [[15121491](#)] [10.1016/j.amjmed.2003.12.033](#)

Ramires, 2000:

Ramires FJ, Mansur A, Coelho O, Maranhão M, Gruppi CJ, Mady C, Ramires JA, Effect of spironolactone on ventricular arrhythmias in congestive heart failure secondary to idiopathic dilated or to ischemic cardiomyopathy. *Am J Cardiol* 2000;85:1207-11. [[10802002](#)]

EMPHASIS-HF, 2010:

Zannad F, McMurray JJ, Drexler H, Krum H, van Veldhuisen DJ, Swedberg K, Shi H, Vincent J, Pitt B Rationale and design of the Eplerenone in Mild Patients Hospitalization And Survival Study in Heart Failure (EMPHASIS-HF). *Eur J Heart Fail* 2010;12:617-22 [[20388647](#)] [10.1093/eurjhf/hfq049](#)

Zannad F, McMurray JJ, Drexler H, Krum H, van Veldhuisen DJ, Swedberg K, Shi H, Vincent J, Pitt B Rationale and design of the Eplerenone in Mild Patients Hospitalization And Survival Study in Heart Failure (EMPHASIS-HF). *Eur J Heart Fail* 2010;12:617-22 [[20388647](#)] [10.1093/eurjhf/hfq049](#)

Zannad F, McMurray JJ, Krum H, van Veldhuisen DJ, Swedberg K, Shi H, Vincent J, Pocock SJ, Pitt B Eplerenone in Patients with Systolic Heart Failure and Mild Symptoms. *N Engl J Med* 2010 Nov 14;: [[21073363](#)] [10.1056/NEJMoa1009492](#)

EPHESUS, 2003:

Pitt B, White H, Nicolau J, Martinez F, Gheorghide M, Aschermann M, van Veldhuisen DJ, Zannad F, Krum H, Mukherjee R, Vincent J Eplerenone reduces mortality 30 days after randomization following acute myocardial infarction in patients with left ventricular systolic dysfunction and heart failure. *J Am Coll Cardiol* 2005 Aug 2;46:425-31 [[16053953](#)]

Pitt B, Remme W, Zannad F, Neaton J, Martinez F, Roniker B, Bittman R, Hurley S, Kleiman J, Gatlin M Eplerenone, a selective aldosterone blocker, in patients with left ventricular dysfunction after myocardial infarction. *N Engl J Med* 2003 Apr 3;348:1309-21 [[12668699](#)]

REMODEL, :

Weir, :

Agostoni, 2005:

Agostoni P, Magini A, Andreini D, Contini M, Apostolo A, Bussotti M, Cattadori G, Palermo P, Spironolactone improves lung diffusion in chronic heart failure. *Eur Heart J* 2005;26:159-64. [[15618072](#)] [10.1093/eurheartj/ehi023](#)

Farquharson, 2000:

Farquharson CA, Struthers AD, Spironolactone increases nitric oxide bioactivity, improves endothelial vasodilator dysfunction, and suppresses vascular angiotensin I/angiotensin II conversion in patients with chronic heart failure. *Circulation* 2000;101:594-7. [[10673249](#)]

Macdonald, 2004:

Macdonald JE, Kennedy N, Struthers AD, Effects of spironolactone on endothelial function, vascular angiotensin converting enzyme activity, and other prognostic markers in patients with mild heart failure already taking optimal treatment. *Heart* 2004;90:765-70. [[15201246](#)] [10.1136/hrt.2003.017368](#)

MacFadyen, 1997:

MacFadyen RJ, Barr CS, Struthers AD, Aldosterone blockade reduces vascular collagen turnover, improves heart rate variability and reduces early morning rise in heart rate in heart failure patients. *Cardiovasc Res* 1997;35:30-4. [[9302344](#)]

Mottram, 2004:

Mottram PM, Haluska B, Leano R, Cowley D, Stowasser M, Marwick TH, Effect of aldosterone antagonism on myocardial dysfunction in hypertensive patients with diastolic heart failure. *Circulation* 2004;110:558-65. [[15277317](#)] [10.1161/01.CIR.0000138680.89536.A9](#)

RALES, 1998:

Effectiveness of spironolactone added to an angiotensin-converting enzyme inhibitor and a loop diuretic for severe chronic congestive heart failure (the Randomized Aldactone Evaluation Study [RALES]). *Am J Cardiol* 1996;78:902-7 [[8888663](#)]

Pitt B, Zannad F, Remme WJ, Cody R, Castaigne A, Perez A, Palensky J, Wittes J The effect of spironolactone on morbidity and mortality in patients with severe heart failure. Randomized Aldactone Evaluation Study Investigators. *N Engl J Med* 1999;341:709-17 [[10471456](#)]

Pitt D, ACE inhibitor co-therapy in patients with heart failure: rationale for the Randomized Aldactone Evaluation Study (RALES). *Eur Heart J* 1995;16 Suppl N:107-10. [[8682055](#)]

Tsutamoto, 2001:

Tsutamoto T, Wada A, Maeda K, Mabuchi N, Hayashi M, Tsutsui T, Ohnishi M, Sawaki M, Fujii M, Matsumoto T, Matsui T, Kinoshita M, Effect of spironolactone on plasma brain natriuretic peptide and left ventricular remodeling in patients with congestive heart failure. *J Am Coll Cardiol* 2001;37:1228-33. [[11300427](#)]

Yee, 2001:

Yee KM, Pringle SD, Struthers AD, Circadian variation in the effects of aldosterone blockade on heart rate variability and QT dispersion in congestive heart failure. *J Am Coll Cardiol* 2001;37:1800-7. [[11401114](#)]

PIE II, :

Han, 1994:

Han YL, Tong M, Jing QM, Hu XL, Liu JQ, Combined therapy of captopril and spironolactone for refractory congestive heart failure. *Chin Med J (Engl)* 1994;107:688-92. [[7805462](#)]

Bednarz, 2000:

Bednarz B, Cybulski J, Chamiec T, [Comparison of the therapeutic efficacy of spironolactone and furosemide in patients with severe congestive heart failure] *Pol Merkuriusz Lek* 2000;9:519-21. [[11081314](#)]

Bednarz B, Cybulski J, Chamiec T [Comparison of the therapeutic efficacy of spironolactone and furosemide in patients with severe congestive heart failure] *Pol Merkuriusz Lek* 2000 Aug;9:519-21 [[11081314](#)]

Nouvel essai, :

Mauersberger, 1985:

Mauersberger H, Rangoonwala B, Ehrlich E, [Comparative study of 2 diuretic-containing combination preparations in patients with edematous heart failure] *Wien Med Wochenschr* 1985;135:205-13. [[4013351](#)]

2 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.