

Clinical trials of anti hypertensive agents for hypertension in uncomplicated hypertension

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1 direct renin inhibitor

Trial	Treatments	Patients	Trials design and methods
aliskiren vs amlodipine			
ACCELERATE , 2011 [NCT00797862] n=NA follow-up:	-	essential hypertension, were aged 18 years or older, and had systolic blood pressure between 150 and 180 mmHg	
aliskiren vs ramipril			
Andersen , 2008 n=NA follow-up: 26 weeks	aliskiren 150 mg (up to 300mg) daily versus ramipril 5 mg (up to 10mg) daily	-	Parallel groups double blind

References

ACCELERATE, 2011:

Brown MJ, McInnes GT, Papst CC, Zhang J, Macdonald TM Aliskiren and the calcium channel blocker amlodipine combination as an initial treatment strategy for hypertension control (ACCELERATE): a randomised, parallel-group trial. Lancet 2011 Jan 12; [21236483] [10.1016/S0140-6736\(10\)62003-X](https://doi.org/10.1016/S0140-6736(10)62003-X)

Andersen, 2008:

Andersen K, Weinberger MH, Egan B, Constance CM, Ali MA, Jin J, Keefe DL Comparative efficacy and safety of aliskiren, an oral direct renin inhibitor, and ramipril in hypertension: a 6-month, randomized, double-blind trial. J Hypertens 2008;26:589-99 [18300872]

2 angiotensin receptor blocker

Trial	Treatments	Patients	Trials design and methods
candesartan vs conventional treatment			
E-COST , 2005 n=1053/995 follow-up:	candesartan, 2 to 12 mg daily versus conventional antihypertensive drugs other than angiotensin converting enzyme inhibitors or ARBs	Japanese essential hypertensive subjects (sitting blood pressure 140-180/90-110 mmHg) aged 35-79 years	Parallel groups single-blind Japan
candesartan vs hydrochlorothiazide			

continued...

Trial	Treatments	Patients	Trials design and methods
ALPINE , 2003 n=197/196 follow-up: 1 year	candesartan versus hydrochlorothiazide	newly detected hypertensives	Parallel groups double-blind Sweden

References

E-COST, 2005:

Suzuki H, Kanno Y Effects of candesartan on cardiovascular outcomes in Japanese hypertensive patients. *Hypertens Res* 2005;28:307-14 [[16138560](#)] [10.1291/hyres.28.307](#)

ALPINE, 2003:

Lindholm LH, Persson M, Alaupovic P, Carlberg B, Svensson A, Samuelsson O Metabolic outcome during 1 year in newly detected hypertensives: results of the Antihypertensive Treatment and Lipid Profile in a North of Sweden Efficacy Evaluation (ALPINE study). *J Hypertens* 2003;21:1563-74 [[12872052](#)] [10.1097/01.hjh.0000084723.53355.76](#)

3 beta-blockers

Trial	Treatments	Patients	Trials design and methods
atenolol vs control			
Coope , 1986 n=419/465 follow-up: 44y	atenolol and bendrofluazide , Atenolol versus Open control	patients aged 60 to 79 years	Parallel groups open
atenolol vs placebo			
MRC I (vs placebo) , 1985 n=4403/8654 follow-up: 5.5y	Propranolol versus Placebo	men and women aged 35-64 yearswith mild hypertension (diastolic pressure 90-109 mm Hg	Parallel groups double blind
MRC old (vs placebo) , 1992 n=1102/2213 follow-up: 5.8y	Atenolol versus Placebo	patients aged 65-74	double blind UK
oxprenolol vs placebo			
IPPPSH , 1985 n=3185/3172 follow-up: 40y	Oxprenolol versus Placebo	men and women aged 40-64 years with uncomplicated essential hypertension (diastolic blood pressures 100-125 mmHg)	Parallel groups Double blind
various beta-blockers vs placebo			
STOP , 1991 n=812/815 follow-up: 21y	active antihypertensive therapy (Thiazide and amiloride or beta-blocker) , Atenolol, Metoprolol, Pindolol, HCTZ/Ami versus Placebo	hypertensive men and women aged 70-84 years	Double blind Swezen
atenolol vs bendroflumethiazide			
MRC I (vs diuretics) , 1985 n=4403/4297 follow-up: 55y	Propranolol versus Bendroflumethiazide.	men and women aged 35-64 years with mild hypertension (diastolic pressure 90-109 mm Hg	Parallel groups double blind
propranolol vs bendroflumethiazide			

continued...

Trial	Treatments	Patients	Trials design and methods
Berglund , 1986 n=NA follow-up: 10y	Propranolol versus Bendroflumethiazide.	patients 21 to 70 years with essential hypertension (sitting diastolic blood pressures 100-120 mm Hg)	
various beta-blockers vs diuretics			
Yurenev , 1992 n=150/154 follow-up: 40y	hypotensive drugs including beta-blockers versus same combination of drugs including diuretics	hypertensive patients with different degrees of left ventricular hypertrophy (LVH)	
HAPPHY , 1988 n=3297/3272 follow-up: 38y	Atenolol, Metoprolol, Propranolol versus Hydrochlorothiazide, Bendroflumethiazide	Men aged 40-64 years with mild to moderate hypertension (diastolic blood pressure 100-130 mmHg) without previous CHD, stroke	open
atenolol vs hydrochlorothiazide+amiloride			
MRC old (vs diuretics) , 1992 n=1102/1081 follow-up: 58y	Atenolol versus Hydrochlorothiazide/amiloride	hypertensive patients aged 65-74	double blind UK

References

Coope, 1986:

Coope J, Warrender TS Randomised trial of treatment of hypertension in elderly patients in primary care. Br Med J (Clin Res Ed) 1986 Nov 1;293:1145-51 [[3094811](#)]

MRC I (vs placebo), 1985:

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MRC old (vs placebo), 1992:

Medical Research Council trial of treatment of hypertension in older adults: principal results. MRC Working Party. BMJ 1992 Feb 15;304:405-12 [[1445513](#)]

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Cardiovascular risk and risk factors in a randomized trial of treatment based on the beta-blocker oxprenolol: the International Prospective Primary Prevention Study in Hypertension (IPPPSH). The IPPPSH Collaborative Group. J Hypertens 1985 Aug;3:379-92 [[2864374](#)]

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MRC old (vs diuretics), 1992:

Medical Research Council trial of treatment of hypertension in older adults: principal results. MRC Working Party. BMJ 1992;304:405-12 [[1445513](#)]

4 calcium-channel blockers

Trial	Treatments	Patients	Trials design and methods
nitrendipine vs placebo			
SYST-EUR , 1997 n=2398/2297 follow-up: 26y	nitrendipine 10-40 mg daily , nitrendipine 10-40 mg daily versus placebo	HBP, >=60 years	Parallel groups Double aveugle 23 countries across Europe
lacidipine vs atenolol			
ELSA , 2002 n=1177/1157 follow-up: 40y	Lacidipine versus atenolol	patients with hypertension	Parallel groups Double blind
lacidipine vs chlorthalidone			
SHELL , 2003 n=NA follow-up: 36?y	lacidipine 4 mg/d versus chlorthalidone 12.5 mg/d	elderly patients with isolated systolic hypertension >or = 60 years	
verapamil vs chlorthalidone			
VHAS , 1998 n=707/707 follow-up: 2 years	verapamil SR 240 mg/d versus chlorthalidone 25mg/d	HBP	Parallel groups Open
diltiazem vs diuretic or beta-blocker			
NORDIL , 2000 n=5410/5471 follow-up: up to 5 years	diltiazem 180-360 daily versus beta-blocker (not specified) or diuretic (not specified)	hypertensive patients, aged 5074 years	Parallel groups Open Norway, Sweden
felopidine or isradipine vs diuretic or beta-blocker			
STOP-2 (CCB vs diuretic or beta-blocker) , 1999 n=2196/2213 follow-up: up to 6 years	felopidine 25 mg or isradipine 25 mg daily versus conventional antihypertensivedrugs (atenolol 50 mg, metoprolol 100 mg,pindolol 5 mg, or hydrochlorothiazide 25 mg plus amiloride2.5 mg daily	patients aged 7084 years with hypertension (blood pressure >180 mm Hg systolic, >105 mm Hg diastolic, or both).	Parallel groups Open
isradipine vs hydrochlorothiazide			
MIDAS , 1996 n=442/441 follow-up: 3y	isradipine 2.5-5.0 mg twice daily versus hydrochlorothiazide 12.5-25 mg Twice daily	HBP	
nicardipine vs trichlormethiazide			
NICS-EH , 1999 n=215/214 follow-up: 4.5 years	Nicardipine SR 20mg twice daily versus trichlormethiazide 2mg once daily	>=60 years of age with systolic blood pressure of 160 to 220 mm Hg and diastolic blood pressure <115 mm Hg	Parallel groups Double blind

References

SYST-EUR, 1997:

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Hansson L, Hedner T, Lund-Johansen P, Kjeldsen SE, Lindholm LH, Syvertsen JO, Lanke J, de Faire U, Dahlof B, Karlberg BE Randomised trial of effects of calcium antagonists compared with diuretics and beta-blockers on cardiovascular morbidity and mortality in hypertension: the Nordic Diltiazem (NORDIL) study. *Lancet* 2000 Jul 29;356:359-65 [10972367]

STOP-2 (CCB vs diuretic or beta-blocker), 1999:

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MIDAS, 1996:

Borhani NO, Mercuri M, Borhani PA, Buckalew VM, Canossa-Terris M, Carr AA, Kappagoda T, Rocco MV, Schnaper HW, Sowers JR, Bond MG Final outcome results of the Multicenter Isradipine Diuretic Atherosclerosis Study (MIDAS). A randomized controlled trial. *JAMA* 1996;276:785-91 [8769587]

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Randomized double-blind comparison of a calcium antagonist and a diuretic in elderly hypertensives. National Intervention Cooperative Study in Elderly Hypertensives Study Group. *Hypertension* 1999 Nov;34:1129-33 [10567194]

5 direct renin inhibitor

Trial	Treatments	Patients	Trials design and methods
aliskiren vs hydrochlorothiazide			
Schmieder (vs HCTZ), 2009 n=567/557 follow-up: 20 weeks	aliskiren 300 mg versus hydrochlorothiazide 25 mg	patients with essential hypertension	Parallel groups double blind

References

Schmieder (vs HCTZ), 2009:

Schmieder RE, Philipp T, Guerediaga J, Gorostidi M, Smith B, Weissbach N, Maboudian M, Botha J, van Ingen H Long-term antihypertensive efficacy and safety of the oral direct renin inhibitor aliskiren: a 12-month randomized, double-blind comparator trial with hydrochlorothiazide. *Circulation* 2009;119:417-25 [19139391]

6 diuretics

Trial	Treatments	Patients	Trials design and methods
High-dose diuretics vs control			
HDFP , 1979 [NCT00000485] n=5485/5455 follow-up: 5 y	High-dose diuretics versus Usual careb	persons with high blood pressure aged 30 to 69 years	US
thiazide diuretics vs control			
Carter , 1970 n=50/49 follow-up: 3.6 y	thiazide versus ?	-	NA Open
Oslo (Hegeland) , 1980 n=406/379 follow-up: 5.5 y	step 1: hydrochlorothiazide 50mg/d, step 2: alpha methyldopa 250-500mg x2/d or propranolol 40-160mg x2/d, versus no treatment	men, aged 40 to 49 years, without target organ damage, with systolic blood pressures between 150 and 179 mm Hg and diastolic blood pressure below 110 mm Hg	parallel group Open Oslo
ANBPS (Australian) , 1980 n=1721/1706 follow-up: 4 y	step 1:chlorothiazide 500 mg/d, step 2: chlorothiazide 500mg x2/d or methyldopa, propranolol, pindolol added, step 3: hydralazine or clonidine added versus placebo (without adjustment according to the BP!)	-	parallel group Double blind Australia
chlorthalidone vs placebo			
SHEP-pilot , 1989 n=443/108 follow-up: 2.8y	chlorthalidone versus placebo	elderly participants with untreated blood pressures of greater than 160/less than 90 mm Hg	double blind
VA-NHLBI , 1977 n=508/504 follow-up: 1.4 y	chlorthalidone 50mg/d versus placebo	patients aged 21 to 50 years with diastolic BP between 85 to 105 mm Hg	Double aveugle USA
SHEP , 1991 [NCT00000514] n=2365/2371 follow-up: 4.4 y	chlorthalidone, 12.5 mg/d , chlorthalidone, 12.5 mg/d , chlorthalidone, 12.5 mg/d versus placebo	patients aged 60 years and above with Systolic BP between 160 and 219 mm Hg and diastolic BP less than 90 mm Hg	Double blind
diuretic and rauwolfia serpentina vs placebo			
USPHS , 1977 n=193/196 follow-up: 7.0 y	diuretic and rauwolfia serpentina versus placebo	subjects, ages 21-55, with diastolic blood pressures between 90 and 115 mm Hg	double blind
High-dose diuretics vs placebo			

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Trial	Treatments	Patients	Trials design and methods
VA II , 1970 n=186/194 follow-up: 3.3y	High-dose diuretics versus Placebo	male hypertensive patients with diastolic blood pressures averaging 90 to 114 mm Hg	
VA-I , 1967 n=73/70 follow-up: 1.5y	High-dose diuretics versus Placebo	-	
Barraclough , 1973 n=58/58 follow-up: 2.0 y	High-dose diuretics versus Placebo	-	
hydrochlorothiazide + amiloride vs placebo			
MRC old , 1992 n=1081/2213 follow-up:	-	hypertensive patients aged 64-75	
hydrochlorothiazide + triamterene vs placebo			
Kuramoto , 1981 n=44/47 follow-up: 4.0y	hydrochlorothiazide + triamterene versus placebo	patients over the age of 60 with sitting diastolic blood pressure on placebo treatment in the range 90-119 mm Hg and a systolic pressure in the range 160-239 mm Hg	double blind
EWPHE , 1985 n=416/424 follow-up: 4.3 y	hydrochlorothiazide + triamterene , hydrochlorothiazide + triamterene versus placebo	patients over the age of 60 with sitting diastolic blood pressure on placebo treatment in the range 90-119 mm Hg and a systolic pressure in the range 160-239 mm Hg	Double blind
thiazide diuretics vs placebo			
MCR 35-64 (diuretics vs pbo) , 1985 n=NA follow-up: 4.9y	bendrofluazide 10 mg/d (step 2: methyl dopa) versus placebo	mild hypertension	Parallel groups single blind
vs			
HAPPY , 1987 n=3272/3297 follow-up: 3.8y	diuretic versus beta-blocker	Men aged 40-64 years with mild to moderate hypertension [diastolic blood pressure (DBP) 100-130 mmHg]	open
High-dose diuretics vs beta-blockers			
MRC (diu vs BB) , 1985 n=4297/4402 follow-up: 4.9y	High-dose diuretics versus -Blockers	-	

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The Australian therapeutic trial in mild hypertension. Report by the Management Committee. *Lancet* 1980;1:1261-7 [[6104081](#)]

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Evaluation of drug treatment in mild hypertension: VA-NHLBI feasibility trial. Plan and preliminary results of a two-year feasibility trial for a multicenter intervention study to evaluate the benefits versus the disadvantages of treating mild hypertension. Prepared for the Veterans Administration-National Heart, Lung, and Blood Institute Study Group for Evaluating Treatment in Mild Hypertension. *Ann N Y Acad Sci* 1978;304:267-92 [[360921](#)]

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Effects of treatment on morbidity in hypertension. II. Results in patients with diastolic blood pressure averaging 90 through 114 mm Hg. *JAMA* 1970 Aug 17;213:1143-52 [[4914579](#)]

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Control of moderately raised blood pressure. Report of a co-operative randomized controlled trial. *Br Med J* 1973;3:434-6 [[4580022](#)]

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MRC (diu vs BB), 1985:

7 endopeptidase inhibitors

Trial	Treatments	Patients	Trials design and methods
LCZ696 vs placebo			
Ruilope , 2010 n=NA follow-up: 8 weeks	LCZ696 for 8 weeks versus placebo	patients with mild to moderate hypertension	Parallel groups double blind 18 countries

References

Ruilope, 2010:

Ruilope LM, Dukat A, Bhm M, Lacourcire Y, Gong J, Lefkowitz MP Blood-pressure reduction with LCZ696, a novel dual-acting inhibitor of the angiotensin II receptor and neprilysin: a randomised, double-blind, placebo-controlled, active comparator study. Lancet 2010 Mar 15;: [20236700] 10.1016/S0140-6736(09)61966-8

8 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.

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