

# 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
<b>aliskiren vs amlodipine</b>			
<b>ACCELERATE , 2011</b> [NCT00797862] n=NA follow-up:	-	essential hypertension, were aged 18 years or older, and had systolic blood pressure between 150 and 180 mmHg	
<b>aliskiren vs ramipril</b>			
<b>Andersen , 2008</b> 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
<b>candesartan vs conventional treatment</b>			
<b>E-COST , 2005</b> 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
<b>candesartan vs hydrochlorothiazide</b>			

continued...

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

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### 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
<b>atenolol vs control</b>			
<b>Coope , 1986</b> n=419/465 follow-up: 44y	atenolol and bendrofluazide , Atenolol versus Open control	patients aged 60 to 79 years	Parallel groups open
<b>atenolol vs placebo</b>			
<b>MRC I (vs placebo) , 1985</b> 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
<b>MRC old (vs placebo) , 1992</b> n=1102/2213 follow-up: 5.8y	Atenolol versus Placebo	patients aged 65-74	double blind UK
<b>oxprenolol vs placebo</b>			
<b>IPPPSH , 1985</b> 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
<b>various beta-blockers vs placebo</b>			
<b>STOP , 1991</b> 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
<b>atenolol vs bendroflumethiazide</b>			
<b>MRC I (vs diuretics) , 1985</b> 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
<b>propranolol vs bendroflumethiazide</b>			

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)	
<b>various beta-blockers vs diuretics</b>			
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
<b>atenolol vs hydrochlorothiazide+amiloride</b>			
MRC old (vs diuretics) , 1992 n=1102/1081 follow-up: 58y	Atenolol versus Hydrochlorothiazide/amiloride	hypertensive patients aged 65-74	double blind UK

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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:

MRC trial of treatment of mild hypertension: principal results. Medical Research Council Working Party. Br Med J (Clin Res Ed) 1985 Jul 13;291:97-104 [[2861880](#)]

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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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### Yurenev, 1992:

Yurenev AP, Dyakonova HG, Novikov ID, Vitols A, Pahl L, Haynemann G, Wallrabe D, Tsifkova R, Romanovska L, Niderle P Management of essential hypertension in patients with different degrees of left ventricular hypertrophy. Multicenter trial. Am J Hypertens 1992;5:182S-189S [[1352979](#)]

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## 4 calcium-channel blockers

Trial	Treatments	Patients	Trials design and methods
<b>nitrendipine vs placebo</b>			
<b>SYST-EUR , 1997</b> 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
<b>lacidipine vs atenolol</b>			
<b>ELSA , 2002</b> n=1177/1157 follow-up: 40y	Lacidipine versus atenolol	patients with hypertension	Parallel groups Double blind
<b>lacidipine vs chlorthalidone</b>			
<b>SHELL , 2003</b> 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	
<b>verapamil vs chlorthalidone</b>			
<b>VHAS , 1998</b> n=707/707 follow-up: 2 years	verapamil SR 240 mg/d versus chlorthalidone 25mg/d	HBP	Parallel groups Open
<b>diltiazem vs diuretic or beta-blocker</b>			
<b>NORDIL , 2000</b> 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
<b>felodipine or isradipine vs diuretic or beta-blocker</b>			
<b>STOP-2 (CCB vs diuretic or beta-blocker) , 1999</b> n=2196/2213 follow-up: up to 6 years	felodipine 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
<b>isradipine vs hydrochlorothiazide</b>			
<b>MIDAS , 1996</b> n=442/441 follow-up: 3y	isradipine 2.5-5.0 mg twice daily versus hydrochlorothiazide 12.5-25 mg Twice daily	HBP	
<b>nicardipine vs trichlormethiazide</b>			
<b>NICS-EH , 1999</b> 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

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Rosei EA, Dal Palu C, Leonetti G, Magnani B, Pessina A, Zanchetti A Clinical results of the Verapamil in Hypertension and Atherosclerosis Study. VHAS Investigators. *J Hypertens* 1997 Nov;15:1337-44 [9383184]

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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
<b>aliskiren vs hydrochlorothiazide</b>			
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

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### 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
<b>High-dose diuretics vs control</b>			
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
<b>thiazide diuretics vs control</b>			
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
<b>chlorthalidone vs placebo</b>			
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
<b>diuretic and rauwolfia serpentina vs placebo</b>			
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
<b>High-dose diuretics vs placebo</b>			

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>VA II , 1970</b> 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	
<b>VA-I , 1967</b> n=73/70 follow-up: 1.5y	High-dose diuretics versus Placebo	-	
<b>Barraclough , 1973</b> n=58/58 follow-up: 2.0 y	High-dose diuretics versus Placebo	-	
<b>hydrochlorothiazide + amiloride vs placebo</b>			
<b>MRC old , 1992</b> n=1081/2213 follow-up:	-	hypertensive patients aged 64-75	
<b>hydrochlorothiazide + triamterene vs placebo</b>			
<b>Kuramoto , 1981</b> 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
<b>EWPHÉ , 1985</b> 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
<b>thiazide diuretics vs placebo</b>			
<b>MCR 35-64 (diuretics vs pbo) , 1985</b> n=NA follow-up: 4.9y	bendrofluazide 10 mg/d (step 2: methyl dopa) versus placebo	mild hypertension	Parallel groups single blind
<b>vs</b>			
<b>HAPPY , 1987</b> 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
<b>High-dose diuretics vs beta-blockers</b>			
<b>MRC (diu vs BB) , 1985</b> n=4297/4402 follow-up: 4.9y	High-dose diuretics versus -Blockers	-	

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MRC (diu vs BB), 1985:

## 7 endopeptidase inhibitors

Trial	Treatments	Patients	Trials design and methods
<b>LCZ696 vs placebo</b>			
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

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## 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.

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.

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