

# Clinical trials of anti hypertensive agents for hypertension in all type of patient

TrialResults-center [www.trialresultscenter.org](http://www.trialresultscenter.org)

## 1 angiotensin-converting enzyme inhibitors

Trial	Treatments	Patients	Trials design and methods
<b>lisinopril vs amlodipine</b>			
<b>ALLHAT (ACEI vs amlodipine) , 2002</b> n=9054/9048 follow-up: 4.9 y	Lisinopril 10 to 40 mg/d versus amlodipine 2.5 to 10 mg/d	participants aged 55 years or older with hypertension and at least 1 other CHD risk fact	Parallel groups Double blind US

## References

### ALLHAT (ACEI vs amlodipine), 2002:

Major outcomes in high-risk hypertensive patients randomized to angiotensin-converting enzyme inhibitor or calcium channel blocker vs diuretic: The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). JAMA 2002;288:2981-97 [[12479763](#)]

Norris K, Bourgoigne J, Gassman J, Hebert L, Middleton J, Phillips RA, Randall O, Rostand S, Sherer S, Toto RD, Wright JT Jr, Wang X, Greene T, Appel LJ, Lewis J Cardiovascular outcomes in the African American Study of Kidney Disease and Hypertension (AASK) Trial. Am J Kidney Dis 2006;48:739-51 [[17059993](#)] [10.1053/j.ajkd.2006.08.004](#)

## 2 direct renin inhibitor

Trial	Treatments	Patients	Trials design and methods
<b>aliskiren vs amlodipine</b>			
<b>ACCELERATE , 2011</b> [ <a href="#">NCT00797862</a> ] n=NA follow-up:	-	essential hypertension, were aged 18 years or older, and had systolic blood pressure between 150 and 180 mm8200;Hg	
<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](#)

### 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](#)]

### 3 angiotensin receptor blocker

Trial	Treatments	Patients	Trials design and methods
<b>ARBs vs control</b>			
<a href="#">Suzuki , 2008</a> n=183/183 follow-up:	ARBs (valsartan, candesartan, and losartan) versus no ARBs	patients with diabetes and chronic kidney disease on dialysis	Parallel groups open
<b>candesartan vs control</b>			
<a href="#">Takahashi , 2006</a> n=43/37 follow-up: 19.4 months	candesartan versus control	patients on chronic haemodialysis in stable condition and with no clinical evidence of cardiac disorders	Parallel groups open
<b>candesartan vs conventional treatment</b>			
<a href="#">E-COST , 2005</a> 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
<a href="#">E-COST-R , 2005</a> n=69/72 follow-up:	candesartan versus conventional treatment	hypertensive subjects 60 to 75 years old with non-diabetic chronic renal insufficiency	Parallel groups open
<a href="#">HIJ-CREATE , 2009</a> n=1024/1025 follow-up: 4.2 y (median)	angiotensin II receptor blocker-based therapy versus non-angiotensin II receptor blocker-based therapy	patients with angiographically documented coronary artery disease and hypertension	Parallel groups open Japan
<b>candesartan vs placebo</b>			
<a href="#">SCOPE , 2003</a> n=2477/2460 follow-up: 3.7 y (mean)	candesartan, 816 mg once daily (target 160/90) versus placebo	patients aged 70-89 years, with systolic blood pressure 160-179 mmHg, and/or diastolic blood pressure 90-99 mmHg, and a Mini Mental State Examination (MMSE) test score >24	Parallel groups double-blind 15 countries
<b>irbesartan vs placebo</b>			
<a href="#">IDNT (irbesartan vs pbo) , 2001</a> n=579/569 follow-up: 2.6 y	Irbesartan 300mg/d (target 135/85) versus placebo	hypertensive patients with nephropathy due to type 2 diabetes	Parallel groups double-blind worldwide
<a href="#">IRMA 2 , 2001</a> n=404/207 follow-up: 2 years	irbesartan 150 mg daily or 300 mg daily versus placebo	hypertensive patients with type 2 diabetes and microalbuminuria	Parallel groups double-blind multinational
<b>losartan vs placebo</b>			

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>RENAAL , 2001</b> n=751/762 follow-up: 3.4 years	lLosartan 50 to 100 mg once daily versus placebo	patients with type 2 diabetes and nephropathy	Parallel groups double-blind
<b>telmisartan vs placebo</b>			
<b>PROPHESSE , 2008</b> [NCT00153062] n=10146/10186 follow-up: 2.5 y	telmisartan 80 mg daily versus placebo	patients who recently had an ischemic stroke	Factorial plan double blind 35 countries
<b>candesartan vs amlodipine</b>			
<b>CASE-J , 2008</b> n=2354/2349 follow-up: 3.2 years	candesartan-based regimen versus amlodipine-based regimen	high-risk Japanese hypertensive patients	Parallel groups open (blinded assessment) Japan
<b>irbesartan vs amlodipine</b>			
<b>IDNT (irbesartan vs amlodipine) , 2001</b> n=579/567 follow-up: 26y	Irbesartan 300mg/d (with a target of 135/85) versus amlodipine 10mg/d (with a target of 135/85)	hypertensive patients with nephropathy due to type 2 diabetes	Parallel groups double-blind worldwide
<b>valsartan vs amlodipine</b>			
<b>VALUE , 2004</b> [NCT00129233] n=7649/7596 follow-up: 4.2 y (mean)	valsartan based regimen versus amlodipine based regimen	patients, aged 50 years or older with treated or untreated hypertension and high risk of cardiac events	Parallel groups Double blind 31 countries
<b>losartan vs atenolol</b>			
<b>LIFE , 2002</b> n=4605/4588 follow-up: 4.8 y (mean)	losartan versus atenolol	patients aged 5580 years, with previously treated or untreated hypertension (sitting blood pressure 160200/95115 mm Hg) and ECG signs of LVH.	Parallel groups Double blind USA, Europe
<b>telmisartan vs enalapril</b>			
<b>DETAIL , 2004</b> n=120/130 follow-up: 5 year	telmisartan 80 mg daily versus enalapril 20 mg daily	subjects with type 2 diabetes and early nephropathy	Parallel groups double-blind
<b>candesartan vs hydrochlorothiazide</b>			
<b>ALPINE , 2003</b> n=197/196 follow-up: 1 year	candesartan versus hydrochlorothiazide	newly detected hypertensives	Parallel groups double-blind Sweden
<b>olmesartan 40 mg vs olmesartan 20 mg plus a calcium-channel blocker</b>			
<b>OSCAR , 2011</b> [NCT00134160] n=578/586 follow-up:	high-dose olmesartan 40 mg per day versus 20-mg/day olmesartan comined with standard dose of amlodipine or azelnidipine	high-risk elderly Japanese hypertension patients	Parallel groups Japan

## References

### **Suzuki, 2008:**

Suzuki H, Kanno Y, Sugahara S, Ikeda N, Shoda J, Takenaka T, Inoue T, Araki R Effect of angiotensin receptor blockers on cardiovascular events in patients undergoing hemodialysis: an open-label randomized controlled trial. *Am J Kidney Dis* 2008;52:501-6 [[18653268](#)] [10.1053/j.ajkd.2008.04.031](#)

### **Takahashi, 2006:**

Takahashi A, Takase H, Toriyama T, Sugiura T, Kurita Y, Ueda R, Dohi Y Candesartan, an angiotensin II type-1 receptor blocker, reduces cardiovascular events in patients on chronic haemodialysis—a randomized study. *Nephrol Dial Transplant* 2006;21:2507-12 [[16766543](#)] [10.1093/ndt/gfl293](#)

### **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/hyPRES.28.307](#)

### **E-COST-R, 2005:**

Nakamura T, Kanno Y, Takenaka T, Suzuki H An angiotensin receptor blocker reduces the risk of congestive heart failure in elderly hypertensive patients with renal insufficiency. *Hypertens Res* 2005;28:415-23 [[16156505](#)] [10.1291/hyPRES.28.415](#)

### **HIJ-CREATE, 2009:**

Kasanuki H, Hagiwara N, Hosoda S, Sumiyoshi T, Honda T, Haze K, Nagashima M, Yamaguchi J, Origasa H, Urashima M, Ogawa H Angiotensin II receptor blocker-based vs. non-angiotensin II receptor blocker-based therapy in patients with angiographically documented coronary artery disease and hypertension: the Heart Institute of Japan Candesartan Randomized Trial for Evaluation in Coronary Artery Disease (HIJ-CREATE). *Eur Heart J* 2009;30:1203-12 [[19346521](#)] [10.1093/eurheartj/ehp101](#)

### **SCOPE, 2003:**

Saxby BK, Harrington F, Wesnes KA, McKeith IG, Ford GA Candesartan and cognitive decline in older patients with hypertension: a substudy of the SCOPE trial. *Neurology* 2008;70:1858-66 [[18458219](#)] [10.1212/01.wnl.0000311447.85948.78](#)

Lithell H, Hansson L, Skoog I, Elmfeldt D, Hofman A, Olofsson B, Trenkwalder P, Zanchetti A The Study on Cognition and Prognosis in the Elderly (SCOPE): principal results of a randomized double-blind intervention trial. *J Hypertens* 2003;21:875-86 [[12714861](#)] [10.1097/01.hjh.0000059028.82022.89](#)

### **IDNT (irbesartan vs pbo), 2001:**

Lewis EJ, Hunsicker LG, Clarke WR, Berl T, Pohl MA, Lewis JB, Ritz E, Atkins RC, Rohde R, Raz I Renoprotective effect of the angiotensin-receptor antagonist irbesartan in patients with nephropathy due to type 2 diabetes. *N Engl J Med* 2001;345:851-60 [[11565517](#)]

Lewis EJ, Hunsicker LG, Clarke WR, Berl T, Pohl MA, Lewis JB, Ritz E, Atkins RC, Rohde R, Raz I Renoprotective effect of the angiotensin-receptor antagonist irbesartan in patients with nephropathy due to type 2 diabetes. *N Engl J Med* 2001;345:851-60 [[11565517](#)]

### **IRMA 2, 2001:**

Parving HH, Lehnert H, Brchner-Mortensen J, Gomis R, Andersen S, Arner P The effect of irbesartan on the development of diabetic nephropathy in patients with type 2 diabetes. *N Engl J Med* 2001;345:870-8 [[11565519](#)] [10.1056/NEJMoa011489](#)

### **RENAAL, 2001:**

Brenner BM, Cooper ME, de Zeeuw D, Keane WF, Mitch WE, Parving HH, Remuzzi G, Snapinn SM, Zhang Z, Shahinfar S Effects of losartan on renal and cardiovascular outcomes in patients with type 2 diabetes and nephropathy. *N Engl J Med* 2001;345:861-9 [[11565518](#)]

### **PROPELLS, 2008:**

Yusuf S, Diener HC, Sacco RL, Cotton D, Ounpuu S, Lawton WA, Palesch Y, Martin RH, Albers GW, Bath P, Bornstein N, Chan BP, Chen ST, Cunha L, Dahlf B, De Keyser J, Donnan GA, Estol C, Gorelick P, Gu V, Hermansson K, Hilbrich L, Kaste M, Lu C, Machnig T, — *N Engl J Med* 2008;359:1225-37 [[18753639](#)] [10.1056/NEJMoa0804593](#)

### **CASE-J, 2008:**

Ogihara T, Nakao K, Fukui T, Fukiyama K, Ueshima K, Oba K, Sato T, Saruta T Effects of candesartan compared with amlodipine in hypertensive patients with high cardiovascular risks: candesartan antihypertensive survival evaluation in Japan trial. *Hypertension* 2008 Feb;51:393-8 [[18172059](#)] [10.1161/HYPERTENSIONAHA.107.098475](#)

### **IDNT (irbesartan vs amlodipine), 2001:**

Lewis EJ, Hunsicker LG, Clarke WR, Berl T, Pohl MA, Lewis JB, Ritz E, Atkins RC, Rohde R, Raz I Renoprotective effect of the angiotensin-receptor antagonist irbesartan in patients with nephropathy due to type 2 diabetes. *N Engl J Med* 2001;345:851-60 [[11565517](#)]

**VALUE, 2004:**

Julius S, Kjeldsen SE, Weber M, Brunner HR, Ekman S, Hansson L, Hua T, Laragh J, McInnes GT, Mitchell L, Plat F, Schork A, Smith B, Zanchetti A Outcomes in hypertensive patients at high cardiovascular risk treated with regimens based on valsartan or amlodipine: the VALUE randomised trial. *Lancet* 2004 Jun 19;363:2022-31 [[15207952](#)]

**LIFE, 2002:**

Dahlof B, Devereux RB, Kjeldsen SE, Julius S, Beevers G, de Faire U, Fyhrquist F, Ibsen H, Kristiansson K, Lederballe-Pedersen O, Lindholm LH, Nieminen MS, Omvik P, Oparil S, Wedel H Cardiovascular morbidity and mortality in the Losartan Intervention For Endpoint reduction in hypertension study (LIFE): a randomised trial against atenolol. *Lancet* 2002 Mar 23;359:995-1003 [[11937178](#)]

**DETAIL, 2004:**

Barnett AH, Bain SC, Bouter P, Karlberg B, Madsbad S, Jervell J, Mustonen J Angiotensin-receptor blockade versus converting-enzyme inhibition in type 2 diabetes and nephropathy. *N Engl J Med* 2004;351:1952-61 [[15516696](#)] [10.1056/NEJMoa042274](#)

**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](#)

**OSCAR, 2011:**

Ogawa H, Kim-Mitsuyama S, Jinnouchi T, Matsui K, Arakawa K Rationale, design and patient baseline characteristics of OlmeSartan and calcium antagonists randomized (OSCAR) study: a study comparing the incidence of cardiovascular events between high-dose angiotensin II receptor blocker (ARB) monotherapy and combination therapy of ARB with calcium channel blocker in Japanese elderly high-risk hypertensive patients (*ClinicalTrials.gov* no. NCT00134160). *Hypertens Res* 2009;32:575-80 [[19444280](#)] [10.1038/hr.2009.60](#)

## 4 angiotensin-converting enzyme inhibitors

CT

Trial	Treatments	Patients	Trials design and methods
<b>ramipril vs amlodipine</b>			
<a href="#">AASK (ramipril vs amlodipine)</a> , 2002 n=436/217 follow-up: 30 y	ramipril 2.5-10 mg/d versus amlodipine 5-10 mg/d	African Americans aged 18 to 70 years with hypertensive renal disease (GFR, 20-65 mL/min per 1.73 m <sup>2</sup> )	Parallel groups Double blind US
<b>various ACEI vs calcium-channel blocker</b>			
<a href="#">STOP-2 (ACEI vs felodipine or isradipine)</a> , 1999 n=2205/2196 follow-up: 50 y	Enalapril or lisinopril, enalapril 10 mg or lisinopril 10 mg daily versus felodipine 2.5 mg or isradipine 2-5 mg daily	patients aged 70-84 years with hypertension (blood pressure >or = 180 mm Hg systolic, >or = 105 mm Hg diastolic, or both)	Parallel groups Open Sweden
<b>captopril vs diuretic or beta-blocker</b>			
<a href="#">CAPPP</a> , 1999 n=5492/5493 follow-up: 6.1 y	captopril 50mg/d versus beta-blocker (not specified) or diuretic (not specified)	Patients aged 25-66 years with a measured diastolic bloodpressure of 100 mm Hg or more on two occasions	Parallel groups Open Sweden and Finland

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>UKPDS-HDS , 1998</b> n=400/358 follow-up: 84 y	captopril started at 25mg twice daily up to 50 mg twice daily (target blood pressure of <150/<85 mmHG) versus atenolol started at 50mg daily up to 100mg if required(target blood pressure of <150/<85 mmHG)	HBP+DM	Parallel groups Open England, Scotland, and Northern Ireland
<b>various ACEI vs diuretic or beta-blocker</b>			
<b>STOP 2 (ACEI vs diuretic or beta-blocker) , 1999</b> n=2205/2213 follow-up: 5.0 y	enalapril 10 mg or lisinopril 10 mg daily versus conventional antihypertensive drugs (atenolol 50 mg, metoprolol 100 mg, pindolol 5 mg, or hydrochlorothiazide 25 mg plus amiloride 25 mg daily)	patients aged 70-84 years with hypertension (blood pressure >180 mm Hg systolic, >105 mm Hg diastolic, or both).	Parallel groups Open Sweden
<b>enalapril vs diuretics</b>			
<b>ANBP2 , 2003</b> n=3044/3039 follow-up: 4.1 y	enalapril versus hydrochlorothiazide	subjects with hypertension 65 to 84 years	Parallel groups open Australia
<b>lisinopril vs diuretics</b>			
<b>ALLHAT (ACEI vs chlorthalidone) , 2002</b> n=9054/15255 follow-up: 49 y	lisinopril 10 to 40 mg/d versus chlorthalidone 12.5 to 25 mg/d	participants aged 55 years or older with hypertension and at least 1 other CHD risk factor	Parallel groups Double blind US
<b>ramipril vs metoprolol</b>			
<b>AASK (ramipril vs metoprolol) , 2002</b> n=436/441 follow-up: 41 y	ramipril 2.5-10 mg/d versus metoprolol 50-200 mg/d	African Americans aged 18 to 70 years with hypertensive renal disease (GFR, 20-65 mL/min per 1.73 m <sup>2</sup> )	Parallel groups Double blind US
<b>various ACEI vs nifedipine</b>			
<b>JMIC-B , 2002</b> n=NA follow-up: 30 y	ACE inhibitor versus nifedipine	HBP+CHD	Parallel groups Open Japan
<b>enalapril vs nisoldipine</b>			
<b>ABCD (H) , 1998</b> n=235/235 follow-up: 53 y	enalapril versus nisoldipine	patients with non-insulin-dependent diabetes and hypertension	double blind

## References

### AASK (ramipril vs amlodipine), 2002:

Wright JT Jr, Bakris G, Greene T, Agodoa LY, Appel LJ, Charleston J, Cheek D, Douglas-Baltimore JG, Gassman J, Glassock R, Hebert L, Jamerson K, Lewis J, Phillips RA, Toto RD, Middleton JP, Rostand SG Effect of blood pressure lowering and antihypertensive drug class on progression of hypertensive kidney disease: results from the AASK trial. JAMA 2002;288:2421-31 [12435255]

### STOP-2 (ACEI vs felodipine or isradipine), 1999:

Hansson L, Lindholm LH, Ekblom T, Dahlöf B, Lanke J, Schersten 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 Nov 20;354:1751-6 [10577635]

**CAPPP, 1999:**

Hansson L, Lindholm LH, Niskanen L, Lanke J, Hedner T, Niklason A, Luomanmaki K, Dahlöf B, de Faire U, Morlin C, Karlberg BE, Wester PO, Björck JE Effect of angiotensin-converting-enzyme inhibition compared with conventional therapy on cardiovascular morbidity and mortality in hypertension: the Captopril Prevention Project (CAPPP) randomised trial. *Lancet* 1999 Feb 20;353:611-6 [10030325]

**UKPDS-HDS, 1998:**

Efficacy of atenolol and captopril in reducing risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 39. UK Prospective Diabetes Study Group. *BMJ* 1998 Sep 12;317:713-20 [9732338]

Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38. UK Prospective Diabetes Study Group. *BMJ* 1998 Sep 12;317:703-13 [9732337]

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

Hansson L, Lindholm LH, Ekblom T, Dahlöf 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 Nov 20;354:1751-6 [10577635]

**ANBP2, 2003:**

Wing LM, Reid CM, Ryan P, Beilin LJ, Brown MA, Jennings GL, Johnston CI, McNeil JJ, Macdonald GJ, Marley JE, Morgan TO, West MJ A comparison of outcomes with angiotensin-converting-enzyme inhibitors and diuretics for hypertension in the elderly. *N Engl J Med* 2003;348:583-92 [12584366]

**ALLHAT (ACEI vs chlorthalidone), 2002:**

Major outcomes in high-risk hypertensive patients randomized to angiotensin-converting enzyme inhibitor or calcium channel blocker vs diuretic: The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). *JAMA* 2002;288:2981-97 [12479763]

**AASK (ramipril vs metoprolol), 2002:**

Wright JT Jr, Bakris G, Greene T, Agodoa LY, Appel LJ, Charleston J, Cheek D, Douglas-Baltimore JG, Gassman J, Glasscock R, Hebert L, Jamerson K, Lewis J, Phillips RA, Toto RD, Middleton JP, Rostand SG Effect of blood pressure lowering and antihypertensive drug class on progression of hypertensive kidney disease: results from the AASK trial. *JAMA* 2002;288:2421-31 [12435255]

Norris K, Bourgoigne J, Gassman J, Hebert L, Middleton J, Phillips RA, Randall O, Rostand S, Sherer S, Toto RD, Wright JT Jr, Wang X, Greene T, Appel LJ, Lewis J Cardiovascular outcomes in the African American Study of Kidney Disease and Hypertension (AASK) Trial. *Am J Kidney Dis* 2006;48:739-51 [17059993] 10.1053/j.ajkd.2006.08.004

**JMIC-B, 2002:**

Yui Y, Sumiyoshi T, Kodama K.itm Long-term effects of nifedipine retard vs ACE inhibitors in hypertension with coronary heart disease: final report of JMIC-B *Circ J* 2002; 66 (suppl): 357

**ABCD (H), 1998:**

Estacio RO, Jeffers BW, Hiatt WR, Biggerstaff SL, Gifford N, Schrier RW The effect of nisoldipine as compared with enalapril on cardiovascular outcomes in patients with non-insulin-dependent diabetes and hypertension. *N Engl J Med* 1998 Mar 5;338:645-52 [9486993]

## 5 beta-blockers

Trial	Treatments	Patients	Trials design and methods
<b>atenolol vs control</b>			
Coope , 1986 n=419/465 follow-up: 44y	atenolol and bendrofluazide , Atenolol versus Open control	patients aged 60 to 79 years	Parallel groups open

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>atenolol vs placebo</b>			
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
Dutch TIA , 1993 n=732/741 follow-up: 26y	Atenolol 50mg/d versus Placebo	aspirin-treated patients with transient ischemic attack or nondisabling ischemic stroke	double blind
TEST , 1995 n=372/348 follow-up: 26y	Atenolol versus Placebo	post stroke	
<b>oxprenolol vs placebo</b>			
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
<b>various beta-blockers vs placebo</b>			
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
<b>atenolol vs bendroflumethiazide</b>			
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
<b>propranolol vs bendroflumethiazide</b>			
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



## 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:

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]

### 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]

### Dutch TIA, 1993:

Trial of secondary prevention with atenolol after transient ischemic attack or nondisabling ischemic stroke. The Dutch TIA Trial Study Group. Stroke 1993 Apr;24:543-8 [8465360]

### TEST, 1995:

Eriksson S, Olofsson BO, Wester PO. imag Atenolol in the secondary prevention after stroke Cerebrovasc Dis 1995; 5: 2125

### IPPPSH, 1985:

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]

### STOP, 1991:

Dahlf B, Lindholm LH, Hansson L, Scherstn B, Ekbohm T, Wester PO Morbidity and mortality in the Swedish Trial in Old Patients with Hypertension (STOP-Hypertension) Lancet 1991;338:1281-5 [1682683]

### MRC I (vs diuretics), 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]

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]

### Berglund, 1986:

Buhler FR, Berglund G, Anderson OK, Brunner HR, Scherrer U, van Brummelen P, Distler A, Philipp T, Fogari R, Mimran A Double-blind comparison of the cardioselective beta-blockers bisoprolol and atenolol in hypertension: the Bisoprolol International Multicenter Study (BIMS). J Cardiovasc Pharmacol 1986;8 Suppl 11:S122-7 [2439782]

### 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]

### HAPPHY, 1988:

Wilhelmsen L, Berglund G, Elmfeldt D, Fitzsimons T, Holzgreve H, Hosie J, Hrnkvist PE, Pennert K, Tuomilehto J, Wedel H Beta-blockers versus diuretics in hypertensive men: main results from the HAPPHY trial. J Hypertens 1987;5:561-72 [2892881]

### 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]

## 6 calcium-channel blockers

Trial	Treatments	Patients	Trials design and methods
amlodipine vs placebo			

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>IDNT (amlodipine vs pbo) , 2001</b> n=567/569 follow-up: 26	Amlodipine 10mg/d versus placebo	hypertensive patients with nephropathy due to type 2 diabetes	Parallel groups Double blind
<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>amlodipine vs atenolol</b>			
<b>ASCOT-BPLA , 2005</b> n=9639/9618 follow-up: 5.5 y	amlodipine 510 mg adding perindopril 48 mg as required versus atenolol 50100 mg adding bendroflumethiazide 12525 mg and potassium as required	patients with hypertension who were aged 4079 years and had at least three other cardiovascular risk factors.	Parallel groups open Nordic countries and UK
<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>verapamil vs atenolol</b>			
<b>INVEST (Pepine) , 2003</b> [NCT00133692] n=11267/11309 follow-up: 2.7 y	verapamil sustained release 240mg/d versus atenolol 50mg/d	patients with hypertension and CAD	14 countries
<b>nifedipine vs atenolol+chlorthalidone</b>			
<b>Castel , 1994</b> n=146/205 follow-up:	Nifedipine 20mg/d versus Clonidine 0.15mg/d (n=61) or atenolol 100mg/d + chlorthalidone 25mg/d	-	
<b>amlodipine vs chlorthalidone</b>			
<b>ALLHAT (CCB vs diu) , 2002</b> n=9048/15255 follow-up: 4.9y	Amlodipine 2.5 to 10g/d , Amlodipine 2.5 to 10g/d , Amlodipine 2.5 to 10g/d , versus chlorthalidone 12.5 to 25 mg/d	participants aged 55 years or older with hypertension and at least 1 other CHD risk factor	Double aveugle US
<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

continued...

Trial	Treatments	Patients	Trials design and methods
<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 50-74 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 70-84 years with hypertension (blood pressure >180 mm Hg systolic, >105 mm Hg diastolic, or both).	Parallel groups Open
<b>verapamil vs diuretic or beta-blocker</b>			
<b>CONVINCE , 2003</b> n=8241/8361 follow-up: 3 y	controlled-onset extendedrelease(COER) verapamil 180mg/d versus hydrochlorothiazide 12.5 mg/d or atenolol 50 mg/d(investigator choice prior to randomization)	hypertension with 1 or more additional risk factors for cardiovascular disease	Parallel groups Double blind 15 countries
<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>amlodipine plus benazepril vs hydrochlorothiazide plus benazepril</b>			
<b>ACCOMPLISH , 2008</b> [NCT00170950] n=5744/5762 follow-up: 36 months	benazepril 40mg plus amlodipine 5mg daily versus benazepril 40mg plus hydrochlorothiazide 12.5mg daily	patients with hypertension who were at high risk for cardiovascular events	Parallel groups double blind US, Sweden, Norway, Denmark, Finland
<b>nifedipine vs hydrochlorothiazide+amiloride</b>			
<b>INSIGHT , 2000</b> n=3157/3164 follow-up: at least 3 years	nifedipine GITS 30mg/d versus hydrochlorothiazide 25mg/d + amiloride 2.5mg/d	HBP + RF	Parallel groups Double blind
<b>amlodipine vs lisinopril</b>			
<b>ALLHAT (CCB vs ACEI) , 2002</b> n=9048/9054 follow-up: 4.9y	Amlodipine 2.5 to 10g/d , Amlodipine 2.5 to 10g/d , Amlodipine 2.5 to 10g/d versus lisinopril 10 to 40 mg/d	participants aged 55 years or older with hypertension and at least 1 other CHD risk factor	Parallel groups Double aveugle US
<b>amlodipine vs metoprolol</b>			
<b>AASK (amlodipine vs metoprolol) , 2002</b> n=217/441 follow-up: 30y	Amlodipine 5-10 mg/d versus metoprolol 50-200 mg/d	African Americans aged 18 to 70 years with hypertensive renal disease (GFR, 20-65 mL/min per 1.73m2)	US
<b>amlodipine vs ramipril</b>			

continued...

Trial	Treatments	Patients	Trials design and methods
<b>AASK (amlodipine vs ramipril) , 2002</b> n=217/436 follow-up: 30	Amlodipine 5-10 mg/d versus ramipril 2.5-10 mg/d	African Americans aged 18 to 70 years with hypertensive renal disease (GFR, 20-65 mL/min per 1.73m <sup>2</sup> )	Factorial plan Double blind US
<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

## References

### **IDNT (amlodipine vs pbo), 2001:**

Lewis EJ, Hunsicker LG, Clarke WR, Berl T, Pohl MA, Lewis JB, Ritz E, Atkins RC, Rohde R, Raz I Renoprotective effect of the angiotensin-receptor antagonist irbesartan in patients with nephropathy due to type 2 diabetes. *N Engl J Med* 2001;345:851-60 [[11565517](#)]

### **SYST-EUR, 1997:**

Staessen JA, Fagard R, Thijs L, Celis H, Arabidze GG, Birkenhager WH, Bulpitt CJ, de Leeuw PW, Dollery CT, Fletcher AE, Forette F, Leonetti G, Nachev C, O'Brien ET, Rosenfeld J, Rodicio JL, Tuomilehto J, Zanchetti A Randomised double-blind comparison of placebo and active treatment for older patients with isolated systolic hypertension. The Systolic Hypertension in Europe (Syst-Eur) Trial Investigators. *Lancet* 1997 Sep 13;350:757-64 [[9297994](#)]

### **ASCOT-BPLA, 2005:**

Dahlof B, Sever PS, Poulter NR, Wedel H, Beevers DG, Caulfield M, Collins R, Kjeldsen SE, Kristinsson A, McInnes GT, Mehlsen J, Nieminen M, O'Brien E, Ostergren J Prevention of cardiovascular events with an antihypertensive regimen of amlodipine adding perindopril as required versus atenolol adding bendroflumethiazide as required, in the Anglo-Scandinavian Cardiac Outcomes Trial-Blood Pressure Lowering Arm (ASCOT-BPLA): a multicentre randomised controlled trial. *Lancet* 2005 Sep 10-16;366:895-906 [[16154016](#)]

### **ELSA, 2002:**

Zanchetti A, Bond MG, Hennig M, Neiss A, Mancia G, Dal Pal C, Hansson L, Magnani B, Rahn KH, Reid JL, Rodicio J, Safar M, Eckes L, Rizzini P Calcium antagonist lacidipine slows down progression of asymptomatic carotid atherosclerosis: principal results of the European Lacidipine Study on Atherosclerosis (ELSA), a randomized, double-blind, long-term trial. *Circulation* 2002;106:2422-7 [[12417537](#)]

### **INVEST (Pepine), 2003:**

Pepine CJ, Handberg EM, Cooper-DeHoff RM, Marks RG, Kowey P, Messerli FH, Mancia G, Cangiano JL, Garcia-Barreto D, Keltai M, Erdine S, Bristol HA, Kolb HR, Bakris GL, Cohen JD, Parmley WW A calcium antagonist vs a non-calcium antagonist hypertension treatment strategy for patients with coronary artery disease. The International Verapamil-Trandolapril Study (INVEST): a randomized controlled trial. *JAMA* 2003 Dec 3;290:2805-16 [[14657064](#)]

### **Castel, 1994:**

Casiglia E, Spolaore P, Mazza A, Ginocchio G, Colangeli G, Onesto C, Di Menza G, Pegoraro L, Ambrosio GB Effect of two different therapeutic approaches on total and cardiovascular mortality in a Cardiovascular Study in the Elderly (CASTEL). *Jpn Heart J* 1994;35:589-600 [[7830324](#)]

### **ALLHAT (CCB vs diu), 2002:**

Major outcomes in high-risk hypertensive patients randomized to angiotensin-converting enzyme inhibitor or calcium channel blocker vs diuretic: The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). *JAMA* 2002;288:2981-97 [[12479763](#)]

### **SHELL, 2003:**

Malacco E, Mancia G, Rappelli A, Menotti A, Zuccaro MS, Coppini A Treatment of isolated systolic hypertension: the SHELL study results. *Blood Press* 2003;12:160-7 [[12875478](#)]

### **VHAS, 1998:**

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

Zanchetti A, Rosei EA, Dal Palu C, Leonetti G, Magnani B, Pessina A The Verapamil in Hypertension and Atherosclerosis Study (VHAS): results of long-term randomized treatment with either verapamil or chlorthalidone on carotid intima-media thickness. *J Hypertens* 1998 Nov;16:1667-76 [[9856368](#)]

**NORDIL, 2000:**

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:**

Hansson L, Lindholm LH, Ekblom T, Dahlof B, Lanke J, Schersten 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 Nov 20;354:1751-6 [[10577635](#)]

**CONVINCE, 2003:**

Black HR, Elliott WJ, Grandits G, Grambsch P, Lucente T, White WB, Neaton JD, Grimm RH Jr, Hansson L, Lacourciere Y, Muller J, Sleight P, Weber MA, Williams G, Wittes J, Zanchetti A, Anders RJ Principal results of the Controlled Onset Verapamil Investigation of Cardiovascular End Points (CONVINCE) trial. *JAMA* 2003 Apr 23-30;289:2073-82 [[12709465](#)]

**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](#)]

**ACCOMPLISH, 2008:**

Jamerson K, Weber MA, Bakris GL, Dahlf B, Pitt B, Shi V, Hester A, Gupte J, Gatlin M, Velazquez EJ Benazepril plus amlodipine or hydrochlorothiazide for hypertension in high-risk patients. *N Engl J Med* 2008 Dec 4;359:2417-28 [[19052124](#)]

Jamerson KA, Bakris GL, Wun CC, Dahlf B, Lefkowitz M, Manfreda S, Pitt B, Velazquez EJ, Weber MA Rationale and design of the avoiding cardiovascular events through combination therapy in patients living with systolic hypertension (ACCOMPLISH) trial: the first randomized controlled trial to compare the clinical outcome effects of first-line combination therapies in hypertension. *Am J Hypertens* 2004;17:793-801 [[15363822](#)] [10.1016/j.amjhyper.2004.05.004](#)

**INSIGHT, 2000:**

Brown MJ, Palmer CR, Castaigne A, de Leeuw PW, Mancia G, Rosenthal T, Ruilope LM Morbidity and mortality in patients randomised to double-blind treatment with a long-acting calcium-channel blocker or diuretic in the International Nifedipine GITS study: Intervention as a Goal in Hypertension Treatment (INSIGHT). *Lancet* 2000 Jul 29;356:366-72 [[10972368](#)]

**ALLHAT (CCB vs ACEI), 2002:**

Major outcomes in high-risk hypertensive patients randomized to angiotensin-converting enzyme inhibitor or calcium channel blocker vs diuretic: The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). *JAMA* 2002;288:2981-97 [[12479763](#)]

**AASK (amlodipine vs metoprolol), 2002:**

Wright JT Jr, Bakris G, Greene T, Agodoa LY, Appel LJ, Charleston J, Cheek D, Douglas-Baltimore JG, Gassman J, Glasscock R, Hebert L, Jamerson K, Lewis J, Phillips RA, Toto RD, Middleton JP, Rostand SG Effect of blood pressure lowering and antihypertensive drug class on progression of hypertensive kidney disease: results from the AASK trial. *JAMA* 2002;288:2421-31 [[12435255](#)]

**AASK (amlodipine vs ramipril), 2002:**

Wright JT Jr, Bakris G, Greene T, Agodoa LY, Appel LJ, Charleston J, Cheek D, Douglas-Baltimore JG, Gassman J, Glasscock R, Hebert L, Jamerson K, Lewis J, Phillips RA, Toto RD, Middleton JP, Rostand SG Effect of blood pressure lowering and antihypertensive drug class on progression of hypertensive kidney disease: results from the AASK trial. *JAMA* 2002;288:2421-31 [[12435255](#)]

**NICS-EH, 1999:**

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](#)]

## 7 direct renin inhibitor

Trial	Treatments	Patients	Trials design and methods
<b>aliskiren vs placebo</b>			
<b>AVOID , 2008</b> [NCT00097955] n=301/298 follow-up: 6 months	aliskiren (150 mg daily for 3 months, followed by an increase in dosage to 300 mg daily for another 3 months versus placebo	patients with hypertension and type 2 diabetes with nephropathy	Parallel groups double blind 15 countries
<b>aliskiren vs hydrochlorothiazide</b>			
<b>Schmieder (vs HCTZ) , 2009</b> n=567/557 follow-up: 20 weeks	aliskiren 300 mg versus hydrochlorothiazide 25 mg	patients with essential hypertension	Parallel groups double blind
<b>aliskiren vs losartan</b>			
<b>ALLAY , 2009</b> [NCT00219141] n=154/152 follow-up: 9 months	aliskiren 300 mg versus losartan 100 mg	patients with hypertension, increased ventricular wall thickness, and body mass index >25 kg/m <sup>2</sup>	Parallel groups open

## References

### AVOID, 2008:

Parving HH, Persson F, Lewis JB, Lewis EJ, Hollenberg NK Aliskiren combined with losartan in type 2 diabetes and nephropathy. N Engl J Med 2008;358:2433-46 [[18525041](#)]

### 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](#)]

### ALLAY, 2009:

Solomon SD, Appelbaum E, Manning WJ, Verma A, Berglund T, Lukashevich V, Cherif Papst C, Smith BA, Dahlf B Effect of the direct Renin inhibitor aliskiren, the Angiotensin receptor blocker losartan, or both on left ventricular mass in patients with hypertension and left ventricular hypertrophy. Circulation 2009;119:530-7 [[19153265](#)]

## 8 diuretics

Trial	Treatments	Patients	Trials design and methods
<b>vs</b>			
<b>HYVET pilot , 2003</b> n=426/426 follow-up: 1.1y	bendroflumethiazide versus no treatment	patients older than 80 years and with a sustained blood pressure of 160-219/90-109 mmHg	Parallel groups Open 10 European countries
<b>High-dose diuretics vs control</b>			

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>HDFP , 1979</b> [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>			
<b>Carter , 1970</b> n=50/49 follow-up: 3.6 y	thiazide versus ?	-	NA Open
<b>Oslo (Hegeland) , 1980</b> n=406/379 follow-up: 5.5 y	step 1: hydrochlorothiazide 50mg/d, step 2: alpha methyl dopa 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
<b>ANBPS (Australian) , 1980</b> n=1721/1706 follow-up: 4 y	step 1:chlorothiazide 500 mg/d, step 2: chlorothiazide 500mg x2/d or methyl dopa, 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>			
<b>SHEP-pilot , 1989</b> 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
<b>VA-NHLBI , 1977</b> 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
<b>SHEP , 1991</b> [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>deserpidine +methylothiazide vs placebo</b>			
<b>HSCS , 1974</b> n=233/219 follow-up: 2.3y	deserpidine 1mg/d + methylothiazide 10mg/d versus placebo	stroke	Parallel groups Double blind USA
<b>diuretic and rauwolfia serpentina vs placebo</b>			
<b>USPHS , 1977</b> 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>			
<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	

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
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	-	
<b>hydrochlorothiazide + amiloride vs placebo</b>			
MRC old , 1992 n=1081/2213 follow-up:	-	hypertensive patients aged 64-75	
<b>hydrochlorothiazide + triamterene vs placebo</b>			
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
<b>indapamide vs placebo</b>			
HYVET , 2008 [NCT00122811] n=1933/1912 follow-up: 1.8y (median)	indapamide sustained release 1.5 mg/d + perindopril 2-4mg/d to obtain SBP<150 and DBP<80 versus placebo	patients 80 years or older with persistent hypertension defined as a sustained systolic BP of 160 mm Hg or higher	Parallel groups Double blind Western and Eastern Europe, China, Australasia, and North Africa
PATS , 1995 n=2841/2841 follow-up: 2y	indapamide 2.5 mg/d versus placebo	-	Parallel groups Double blind China
<b>thiazide diuretics vs placebo</b>			
MCR 35-64 (diuretics vs pbo) , 1985 n=NA follow-up: 4.9y	bendrofluazide 10 mg/d (step 2: methyldopa) versus placebo	mild hypertension	Parallel groups single blind
<b>High-dose diuretics vs beta-blockers</b>			
MRC (diu vs BB) , 1985 n=4297/4402 follow-up: 4.9y	High-dose diuretics versus -Blockers	-	

## References

### HYVET pilot, 2003:

Bulpitt CJ, Beckett NS, Cooke J, Dumitrascu DL, Gil-Extremera B, Nachev C, Nunes M, Peters R, Staessen JA, Thijs L Results of the pilot study for the Hypertension in the Very Elderly Trial. J Hypertens 2003 Dec;21:2409-17 [14654762]

### HDFP, 1979:



Five-year findings of the hypertension detection and follow-up program. I. Reduction in mortality of persons with high blood pressure, including mild hypertension. Hypertension Detection and Follow-up Program Cooperative Group. JAMA 1979 Dec 7;242:2562-71 [490882]

Five-year findings of the hypertension detection and follow-up program. III. Reduction in stroke incidence among persons with high blood pressure. Hypertension Detection and Follow-up Program Cooperative Group. JAMA 1982 Feb 5;247:633-8 [7033578]

Effect of stepped care treatment on the incidence of myocardial infarction and angina pectoris. 5-Year findings of the hypertension detection and follow-up program. Hypertension 1984 Mar-Apr;6:1198-206 [6724670]

#### **Carter, 1970:**

Carter AB Hypotensive therapy in stroke survivors. Lancet 1970;1:485-9 [4190177]

#### **Oslo (Hegeland), 1980:**

Helgeland A Treatment of mild hypertension: a five year controlled drug trial. The Oslo study. Am J Med 1980;69:725-32 [7001898]

#### **ANBPS (Australian ), 1980:**

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

#### **SHEP-pilot, 1989:**

Perry HM Jr, Smith WM, McDonald RH, Black D, Cutler JA, Furberg CD, Greenlick MR, Kuller LH, Schnaper HW, Schoenberger JA Morbidity and mortality in the Systolic Hypertension in the Elderly Program (SHEP) pilot study. Stroke 1989 Jan;20:4-13 [2911834]

#### **VA-NHLBI, 1977:**

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]

#### **SHEP, 1991:**

Prevention of stroke by antihypertensive drug treatment in older persons with isolated systolic hypertension. Final results of the Systolic Hypertension in the Elderly Program (SHEP). SHEP Cooperative Research Group. JAMA 1991;265:3255-64 [2046107]

Kostis JB, Davis BR, Cutler J, Grimm RH Jr, Berge KG, Cohen JD, Lacy CR, Perry HM Jr, Blafox MD, Wassertheil-Smoller S, Black HR, Schron E, Berkson DM, Curb JD, Smith WM, McDonald R, Applegate WB Prevention of heart failure by antihypertensive drug treatment in older persons with isolated systolic hypertension. SHEP Cooperative Research Group. JAMA 1997;278:212-6 [9218667]

Kostis JB, Cabrera J, Cheng JQ, Cosgrove NM, Deng Y, Pressel SL, Davis BR Association between chlorthalidone treatment of systolic hypertension and long-term survival. JAMA 2011 Dec 21;306:2588-93 [22187278] 10.1001/jama.2011.1821

#### **HSCS, 1974:**

Effect of antihypertensive treatment on stroke recurrence. Hypertension-Stroke Cooperative Study Group. JAMA 1974 Jul 22;229:409-18 [4599980]

Effect of antihypertensive treatment on stroke recurrence. Hypertension-Stroke Cooperative Study Group. JAMA 1974;229:409-18 [4599980]

#### **USPHS, 1977:**

Smith WM. Treatment of mild hypertension: results of a ten-year intervention trial Circ Res. 1977; 40(5 suppl 1):I98-I105.

Smith WM Treatment of mild hypertension: results of a ten-year intervention trial. Circ Res 1977;40:I98-105 [140029]

#### **VA II, 1970:**

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]

#### **VA-I, 1967:**

Dunphy JE Surgery's relevance to an understanding of basic biology. Tissue repair and cellular regeneration. JAMA 1967;202:116-7 [6072204]

#### **Barraclough, 1973:**

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

#### **MRC old, 1992:**

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

**Kuramoto, 1981:****EWPHE, 1985:**

Amery A, Birkenhager W, Brixko P, Bulpitt C, Clement D, Deruyttere M, De Schaepdryver A, Dollery C, Fagard R, Forette F Mortality and morbidity results from the European Working Party on High Blood Pressure in the Elderly trial. *Lancet* 1985 Jun 15;1:1349-54 [[2861311](#)]

**HYVET, 2008:**

Beckett NS, Peters R, Fletcher AE, Staessen JA, Liu L, Dumitrascu D, Stoyanovsky V, Antikainen RL, Nikitin Y, Anderson C, Belhani A, Forette F, Rajkumar C, Thijs L, Banya W, Bulpitt CJ Treatment of Hypertension in Patients 80 Years of Age or Older. *N Engl J Med* 2008 Mar 31;: [[18378519](#)]

**PATS, 1995:**

Post-stroke antihypertensive treatment study. A preliminary result. PATS Collaborating Group. *Chin Med J (Engl)* 1995;108:710-7 [[8575241](#)]

**MCR 35-64 (diuretics vs pbo), 1985:**

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

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

**MRC (diu vs BB), 1985:**

## 9 endopeptidase inhibitors

Trial	Treatments	Patients	Trials design and methods
<b>LCZ696 vs placebo</b>			
<a href="#">Ruilope , 2010</a> 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](#)

## 10 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.