

# Clinical trials of anti hypertensive agents for hypertension in diabetic patients

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## 1 angiotensin receptor blocker

Trial	Treatments	Patients	Trials design and methods
<b>irbesartan vs placebo</b>			
<b>IRMA 2 , 2001</b> 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>IDNT (irbesartan vs pbo) , 2001</b> n=579/569 follow-up: 2.6 years	Irbesartan 300 mg daily versus placebo	hypertensive patients with nephropathy due to type 2 diabetes	Parallel groups double blind Worldwide
<b>IPDM (150mg) , 2001</b> n=195/201 follow-up: 2 years	irbesartan 150 mg daily versus placebo	hypertensive patients with type 2 diabetes and microalbuminuria	Parallel groups double-blind Worldwide
<b>losartan vs placebo</b>			
<b>RENAAL , 2001</b> n=751/762 follow-up: 3.4 y	losartan 50 to 100 mg once daily versus placebo	patients with type 2 diabetes and nephropathy	Parallel groups double-blind America, Europe, Asia
<b>irbesartan vs amlodipine</b>			
<b>IDNT (irbesartan vs amlodipine) , 2001</b> n=579/567 follow-up: 2.6 years	Irbesartan 300 mg daily versus amlodipine 10 mg daily	hypertensive patients with nephropathy due to type 2 diabetes	Parallel groups double blind Worldwide
<b>valsartan vs amlodipine</b>			
<b>NAGOYA HEART , 2011</b> <i>unpublished</i> [NCT00129233] n=575/575 follow-up: 3.2 y median	blood-pressure-lowering therapy based on valsartan; blood-pressure goal of <130/80 mm Hg versus blood-pressure-lowering therapy based on amlodipine; blood-pressure goal of <130/80 mm Hg	patients with hypertension with type 2 diabetes or impaired glucose tolerance	Parallel groups open Japan
<b>losartan vs atenolol</b>			
<b>LIFE (diabetic subgroup) , 2002</b> n=586/609 follow-up: 4.7 years	losartan 50mg daily at step 1 versus atenolol 50mg daily at step 1	patients with diabetes (subgroup) , hypertension, and signs of left-ventricular hypertrophy on electrocardiograms	Parallel groups double-blind USA, UK, Nordic countries
<b>telmisartan vs enalapril</b>			

continued...

Trial	Treatments	Patients	Trials design and methods
<a href="#">DETAIL , 2004</a> 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

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## 2 angiotensin-converting enzyme inhibitors

Trial	Treatments	Patients	Trials design and methods
<a href="#">captopril or atenolol vs control</a>			

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>UKPDS 38 , 1998</b> n=758/390 follow-up: 8.4y (median)	tight control of blood pressure aiming at a BP <150/85 (with the use of captopril or atenolol as main treatment, other treatment were added if the control criteria were not met) versus less tight control aiming at a blood pressure of <180/105 (avoiding treatment with ACE inhibitors or beta-blockers)	hypertensive patients with type 2 diabetes	Parallel groups open UK
<b>ACE inhibitors vs placebo</b>			
<b>HOPE (diabetic subgroup) , 2000</b> n=1808/1759 follow-up: 4.5 years	ramipril 10 mg once per day orally versus placebo	patients with diabetes (sub group), aged 55 years or older, who had a previous cardiovascular event or at least one other cardiovascular risk factor, no clinical proteinuria, heart failure, or low ejection fraction	Factorial plan double-blind North, South america, Europe
<b>captopril vs atenolol</b>			
<b>UKPDS 39 , 1998</b> n=400/358 follow-up: ND	captopril 25 mg/d aiming at a BP <150/85 versus atenolol 50mg/d aiming at a BP <150/85	hypertensive patients with type 2 diabetes	Parallel groups open UK
<b>ACE inhibitor vs calcium-channel blocker</b>			
<b>STOP-2 (ACEI vs CCB) (diabetic subgroup) , 2000</b> n=235/231 follow-up: 5.03y	ACE inhibitor versus calcium antagonists	diabetic (subgroup) elderly patients aged 70-84 years	open with blind assessment Sweden
<b>lisinopril vs chlorthalidone</b>			
<b>ALLHAT (lisi vs chlor, diabetic subgroup) , 2002</b> n=2431/4498 follow-up: 4.9 y	lisinopril 10 to 40 mg/d versus chlorthalidone 12.5 to 25 mg/d	diabetic (subgroup) participants aged 55 years or older with hypertension	Parallel groups double-blind
<b>captopril vs diuretic and/or beta-blockers</b>			
<b>CAPP (diabetic subgroup) , 1999</b> n=309/263 follow-up: 6.1 year	Captopril initial dose of 50 mg daily given in one or two doses versus thiazide diuretic or beta-blocker	Patients aged 25-66 years with a measured diastolic blood pressure of 100 mm Hg or more on two occasions; subgroup of diabetic patients	Parallel groups open with blinded assessment Sweden, Finland
<b>ACE inhibitor vs diuretic or beta-blocker</b>			
<b>STOP-2 (ACEI, diabetic subgroup) , 2000</b> n=235/253 follow-up: 5.03y	ACE inhibitor versus conventional treatment (diuretic or beta-blocker)	diabetic (subgroup) elderly patients aged 70-84 years with hypertension	Parallel groups open with blind assessment Sweden

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#### **ALLHAT (lisi vs chlor, diabetic subgroup), 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]

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## **3 calcium-channel blockers**

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>amlodipine vs placebo</b>			
IDNT (amlodipine vs PBO) , 2001 n=567/569 follow-up: 2.6 years	Amlodipine 10 mg daily versus placebo	hypertensive patients with nephropathy due to type 2 diabetes	Parallel groups double-blind Worldwide
<b>nitrendipine vs placebo</b>			
Syst-Eur (diabetic subgroup) , 1999 n=252/240 follow-up: 2 years	Calcium-channel blocker versus placebo	subgroup of diabetic patients, age, >=60 years) with systolic blood pressure of 160 to 219 mm Hg and diastolic pressure below 95 mm Hg	Parallel groups double blind
<b>benazepril + amlodipine vs benazepril + hydrochlorothiazide</b>			
ACCOMPLISH (diabetic subgroup) , 2010 [NCT00170950] n=1432/1410 follow-up: 36 months	benazepril, combined with amlodipine versus benazepril, combined with hydrochlorothiazide	patients with diabetes (subgroup) and hypertension at high risk of cardiovascular and related events	Parallel groups double-blind US, Norway, Denmark, Finland
<b>amlodipine vs chlorthalidone</b>			
ALLHAT (amlodipine vs chlor, diabetic subgroup) , 2002 n=2664/4498 follow-up: 4.9 y	amlodipine versus chlorthalidone	diabetic (subgroup) participants aged 55 years or older with hypertension	Parallel groups double-blind
<b>nifedipine vs coamilofide</b>			
INSIGHT (diabetic subgroup) , 2000 n=649/653 follow-up: 4 y	Nifedipine GITS 30 mg daily versus co-amilofide hydrochlorothiazide 25 mg plus amiloride 2.5 mg	diabetic (subgroup) patients aged 55-80 years with hypertension (blood pressure >= 150/95 mm Hg, or >= 160 mmHg systolic)	Parallel groups double-blind Europe, Israel
<b>diltiazem vs diuretic and/or beta-blocker</b>			
NORDIL (diabetic subgroup) , 2000 n=351/376 follow-up: 4.5 y	Diltiazem 180/360 mg diltiazem daily at step one versus thiazide diuretic or a beta-blocker at step one	diabetic patients (subgroup), aged 50-74 years who had diastolic blood pressure of 100 mm Hg or more	Parallel groups open Norway, Sweden
<b>calcium-channel blocker vs diuretic or beta-blocker</b>			
STOP-2 (CCB, diabetic subgroup) , 2000 n=231/253 follow-up: 5.03y	Calcium-channel blocker versus diuretic or beta-blocker	diabetic (subgroup) elderly patients aged 70-84 years	Parallel groups open with blind assessment Sweden
<b>felodipine or isradipine vs diuretic or beta-blocker</b>			
STOP-2 (CCB vs diuretic or beta-blocker) , 1999 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 amiloride 2.5 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>nisoldipine vs enalapril</b>			

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

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### **ABCD (hypertension), 1998:**

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## **4 direct renin inhibitor**

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<a href="#">aliskiren</a> vs placebo			

continued...

Trial	Treatments	Patients	Trials design and methods
<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

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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](#)]

## 5 diuretics

Trial	Treatments	Patients	Trials design and methods
<b>chlorthalidone vs placebo</b>			
<b>SHEP (diabetic subgroup) , 1996</b> n=283/300 follow-up: 5 year	low dose of chlorthalidone (12.5-25.0 mg/d) with a step-up to atenolol (25.0-50.0 mg/d) or reserpine (0.05-0.10 mg/d) if needed versus placebo	men and women aged 60 years and older , non-insulin-treated diabetic (sub group) patients with isolated systolic hypertension (systolic BP $\geq$ 160 mm Hg; diastolic BP, $<$ 90 mm Hg)	Parallel groups double-blind

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Curb JD, Pressel SL, Cutler JA, Savage PJ, Applegate WB, Black H, Camel G, Davis BR, Frost PH, Gonzalez N, Guthrie G, Oberman A, Rutan GH, Stamler J Effect of diuretic-based antihypertensive treatment on cardiovascular disease risk in older diabetic patients with isolated systolic hypertension. Systolic Hypertension in the Elderly Program Cooperative Research Group. JAMA 1996;276:1886-92 [[8968014](#)]

## 6 intensive treatment

Trial	Treatments	Patients	Trials design and methods
<b>intensive vs usual</b>			
<b>ACCORD (blood pressure) , 2010</b> [NCT00000620] n=2363/2371 follow-up: 4.7 y	intensive blood-pressure control, targeting a systolic pressure of less than 120 mm Hg versus standard blood-pressure control	high-risk patients with type 2 diabetes, high HbA1c concentrations ( $>$ 7.5% ), and cardiovascular disease (or $\geq$ 2 cardiovascular risk factors)	Factorial plan open United States, Canada



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## 7 Treatment blood pressure target

Trial	Treatments	Patients	Trials design and methods
<b>more intensive blood pressure lowering strategie vs less intensive blood pressure lowering strategie</b>			
<b>ABCD target (H) , 2000</b> n=237/233 follow-up: 5 year	intensive treatment with a diastolic blood pressure goal of 75 mmHg versus moderate treatment with a diastolic blood pressure goal of 80-89 mmHg	diabetes patients with DBP >=90 mmHg	Parallel groups open
<b>ABCD target (N) , 2002</b> n=237/243 follow-up:	intensive treatment (diastolic blood pressure decrease of 10 mmHg below baseline DBP) versus moderate treatment (diastolic blood pressure goal of 80-89 mmHg)	diabetes patients with diastolic blood pressure between 80 and 89mmHg	Parallel groups open

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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.

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.

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