

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

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## 1 ACE inhibitor

Trial	Treatments	Patients	Trials design and methods
<b>captopril or atenolol vs control</b>			
UKPDS 38 , 1998 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 inhibitor vs placebo</b>			
HOPE (diabetic subgroup) , 2000 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>			
UKPDS 39 , 1998 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 CCB</b>			
STOP-2 (ACEI vs CCB) (diabetic subgroup) , 2000 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>			
ALLHAT (lisi vs chlor, diabetic subgroup) , 2002 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>			
CAPP (diabetic subgroup) , 1999 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>			

continued...

Trial	Treatments	Patients	Trials design and methods
<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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## 2 angiotensin receptor blocker

Trial	Treatments	Patients	Trials design and methods
<b>irbesartan vs placebo</b>			
<b>IDNT (vs placebo) , 2001</b> 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
<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 , 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 (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>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>			

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>NAGOYA HEART</b> [NCT00129233] n=1150 follow-up:	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>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>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 , 2002</b> n=4605/4588 follow-up: 4.8 y (mean)	losartan versus atenolol	patients aged 55-80 years, with previously treated or untreated hypertension (sitting blood pressure 160/200/95/115 mm Hg) and ECG signs of LVH.	Parallel groups Double blind USA, Europe
<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>			
<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

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## **3 calcium blockers**

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

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>IDNT amlodipine , 2001</b> 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>			
<b>Syst-Eur (diabetic subgroup) , 1999</b> 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>			
<b>ACCOMPLISH (diabetic subgroup) , 2010</b> [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>			
<b>ALLHAT (amlodipine vs chlor, diabetic subgroup) , 2002</b> 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>			
<b>INSIGHT (diabetic subgroup) , 2000</b> 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>calcium-channel blocker vs diuretic or beta-blocker</b>			
<b>STOP-2 CCB (diabetic subgroup) , 2000</b> 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>diltiazem vs diuretic or beta-blocker</b>			
<b>NORDIL (diabetic subgroup) , 2000</b> 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>nisoldipine vs enalapril</b>			
<b>ABCD hypertension , 1998</b> n=235/235 follow-up: 5 y	nisoldipine (long acting) versus enalapril	patients with non-insulin-dependent diabetes and hypertension	Factorial plan Double blind USA
<b>amlodipine vs fosinopril</b>			

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Trial	Treatments	Patients	Trials design and methods
<b>FACET , 1997</b> n=191/189 follow-up: 3.5 y	amlodipine (long acting) 10 mg daily versus fosinopril 20 mg daily	hypertensive patients with NIDDM	Parallel groups open Italy

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## 4 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

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## 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

## References

### SHEP (diabetic subgroup), 1996:

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

## References

### ACCORD blood pressure, 2010:

Effects of Medical Therapies on Retinopathy Progression in Type 2 Diabetes. N Engl J Med 2010 Jun 29;: [[20587587](#)] [10.1056/NEJMoa1001288](#)

Ismail-Beigi F, Craven T, Banerji MA, Basile J, Calles J, Cohen RM, Cuddihy R, Cushman WC, Genuth S, Grimm RH Jr, Hamilton BP, Hoogwerf B, Karl D, Katz L, Krikorian A, O'Connor P, Pop-Busui R, Schubart U, Simmons D, Taylor H, Thomas A, Weiss D, Hramiak I Effect of intensive treatment of hyperglycaemia on microvascular outcomes in type 2 diabetes: an analysis of the ACCORD randomised trial. Lancet 2010 Jun 29;: [[20594588](#)] [10.1016/S0140-6736\(10\)60576-4](#)

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Cushman WC, Evans GW, Byington RP, Goff DC Jr, Grimm RH Jr, Cutler JA, Simons-Morton DG, Basile JN, Corson MA, Probstfield JL, Katz L, Peterson KA, Friedewald WT, Buse JB, Bigger JT, Gerstein HC, Ismail-Beigi F Effects of intensive blood-pressure control in type 2 diabetes mellitus. N Engl J Med 2010;362:1575-85 [[20228401](#)] [10.1056/NEJMoa1001286](#)

## 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 (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 $\geq$ 90 mmHg	Parallel groups open
<b>ABCD (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

## References

### ABCD (H), 2000:

Estacio RO, Jeffers BW, Gifford N, Schrier RW Effect of blood pressure control on diabetic microvascular complications in patients with hypertension and type 2 diabetes. Diabetes Care 2000;23 Suppl 2:B54-64 [[10860192](#)]

### ABCD (N), 2002:

Schrier RW, Estacio RO, Esler A, Mehler P Effects of aggressive blood pressure control in normotensive type 2 diabetic patients on albuminuria, retinopathy and strokes. Kidney Int 2002;61:1086-97 [[11849464](#)] [10.1046/j.1523-1755.2002.00213.x](#)

## 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.

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.