

# 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><br>n=404/207<br>follow-up: 2 years   | irbesartan 150 mg daily or 300 mg daily<br>versus<br>placebo  | hypertensive patients with type 2 diabetes<br>and microalbuminuria  | Parallel groups<br>double-blind<br>multinational             |
| <b>IDNT (irbesartan vs pbo) , 2001</b><br>n=579/569<br>follow-up: 2.6 years                               | Irbesartan 300 mg daily<br>versus<br>placebo  | hypertensive patients with nephropathy due<br>to type 2 diabetes  | Parallel groups<br>double blind<br>Worldwide                 |
| <b>IPDM (150mg) , 2001</b><br>n=195/201<br>follow-up: 2 years   | irbesartan 150 mg daily<br>versus<br>placebo  | hypertensive patients with type 2 diabetes<br>and microalbuminuria  | Parallel groups<br>double-blind<br>Worldwide                 |
| <b>losartan vs placebo</b>  |   |   |  |
| <b>RENAAL , 2001</b><br>n=751/762<br>follow-up: 3.4 y   | losartan 50 to 100 mg once daily<br>versus<br>placebo   | patients with type 2 diabetes and<br>nephropathy  | Parallel groups<br>double-blind<br>America, Europe, Asia     |
| <b>irbesartan vs amlodipine</b>   |   |   |  |
| <b>IDNT (irbesartan vs amlodipine) , 2001</b><br>n=579/567<br>follow-up: 2.6 years                        | Irbesartan 300 mg daily<br>versus<br>amlodipine 10 mg daily   | hypertensive patients with nephropathy due<br>to type 2 diabetes  | Parallel groups<br>double blind<br>Worldwide                 |
| <b>valsartan vs amlodipine</b>  |   |   |  |
| <b>NAGOYA HEART , 2011</b><br><i>unpublished</i><br>[NCT00129233]<br>n=575/575<br>follow-up: 3.2 y median | blood-pressure-lowering therapy based on<br>valsartan; blood-pressure goal of <130/80<br>mm Hg<br>versus<br>blood-pressure-lowering therapy based on<br>amlodipine; blood-pressure goal of <130/80<br>mm Hg | patients with hypertension with type 2<br>diabetes or impaired glucose tolerance  | Parallel groups<br>open<br>Japan                             |
| <b>losartan vs atenolol</b>   |   |   |  |
| <b>LIFE (diabetic subgroup) , 2002</b><br>n=586/609<br>follow-up: 4.7 years                               | losartan 50mg daily at step 1<br>versus<br>atenolol 50mg daily at step 1  | patients with diabetes (subgroup) ,<br>hypertension, and signs of left-ventricular<br>hypertrophy on electrocardiograms | Parallel groups<br>double-blind<br>USA, UK, Nordic countries |
| <b>telmisartan vs enalapril</b>   |   |   |  |

continued...

| Trial  | Treatments   | Patients  | Trials design and methods       |
|--|--|---|---------------------------------|
| <a href="#">DETAIL, 2004</a><br>n=120/130<br>follow-up: 5 year | telmisartan 80 mg daily<br>versus<br>enalapril 20 mg daily | subjects with type 2 diabetes and early nephropathy | Parallel groups<br>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><br>n=758/390<br>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)<br>versus<br>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<br>open<br>UK                                      |
| <b>ACE inhibitors vs placebo</b>   |  |  |  |
| <b>HOPE (diabetic subgroup) , 2000</b><br>n=1808/1759<br>follow-up: 4.5 years              | ramipril 10 mg once per day orally<br>versus<br>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<br>double-blind<br>North, South america, Europe     |
| <b>captopril vs atenolol</b>   |  |  |  |
| <b>UKPDS 39 , 1998</b><br>n=400/358<br>follow-up: ND                                       | captopril 25 mg/d aiming at a BP <150/85<br>versus<br>atenolol 50mg/d aiming at a BP <150/85   | hypertensive patients with type 2 diabetes   | Parallel groups<br>open<br>UK                                      |
| <b>ACE inhibitor vs calcium-channel blocker</b>  |  |  |  |
| <b>STOP-2 (ACEI vs CCB) (diabetic subgroup) , 2000</b><br>n=235/231<br>follow-up: 5.03y    | ACE inhibitor<br>versus<br>calcium antagonists   | diabetic (subgroup) elderly patients aged 70-84 years  | open with blind assessment<br>Sweden                               |
| <b>lisinopril vs chlorthalidone</b>  |  |  |  |
| <b>ALLHAT (lisi vs chlor, diabetic subgroup) , 2002</b><br>n=2431/4498<br>follow-up: 4.9 y | lisinopril 10 to 40 mg/d<br>versus<br>chlorthalidone 12.5 to 25 mg/d   | diabetic (subgroup) participants aged 55 years or older with hypertension  | Parallel groups<br>double-blind                                    |
| <b>captopril vs diuretic and/or beta-blockers</b>  |  |  |  |
| <b>CAPP (diabetic subgroup) , 1999</b><br>n=309/263<br>follow-up: 6.1 year                 | Captopril initial dose of 50 mg daily given in one or two doses<br>versus<br>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<br>open with blinded assessment<br>Sweden, Finland |
| <b>ACE inhibitor vs diuretic or beta-blocker</b>   |  |  |  |
| <b>STOP-2 (ACEI, diabetic subgroup) , 2000</b><br>n=235/253<br>follow-up: 5.03y            | ACE inhibitor<br>versus<br>conventional treatment (diuretic or beta-blocker)   | diabetic (subgroup) elderly patients aged 70-84 years with hypertension  | Parallel groups<br>open with blind assessment<br>Sweden            |

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## **3 calcium-channel blockers**

| Trial   | Treatments   | Patients   | Trials design and methods                                       |
|---|--|--|---|
| <b>amlodipine vs placebo</b>  |  |  |   |
| IDNT (amlodipine vs PBO) , 2001<br>n=567/569<br>follow-up: 2.6 years                          | Amlodipine 10 mg daily<br>versus<br>placebo  | hypertensive patients with nephropathy due to type 2 diabetes  | Parallel groups<br>double-blind<br>Worldwide                    |
| <b>nitrendipine vs placebo</b>  |  |  |   |
| Syst-Eur (diabetic subgroup) , 1999<br>n=252/240<br>follow-up: 2 years                        | Calcium-channel blocker<br>versus<br>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<br>double blind                                 |
| <b>benazepril + amlodipine vs benazepril + hydrochlorothiazide</b>                            |  |  |   |
| ACCOMPLISH (diabetic subgroup) , 2010<br>[NCT00170950]<br>n=1432/1410<br>follow-up: 36 months | benazepril, combined with amlodipine<br>versus<br>benazepril, combined with hydrochlorothiazide  | patients with diabetes (subgroup) and hypertension at high risk of cardiovascular and related events                                   | Parallel groups<br>double-blind<br>US, Norway, Denmark, Finland |
| <b>amlodipine vs chlorthalidone</b>   |  |  |   |
| ALLHAT (amlodipine vs chlor, diabetic subgroup) , 2002<br>n=2664/4498<br>follow-up: 4.9 y     | amlodipine<br>versus<br>chlorthalidone   | diabetic (subgroup) participants aged 55 years or older with hypertension  | Parallel groups<br>double-blind                                 |
| <b>nifedipine vs coamilofide</b>  |  |  |   |
| INSIGHT (diabetic subgroup) , 2000<br>n=649/653<br>follow-up: 4 y                             | Nifedipine GITS 30 mg daily<br>versus<br>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<br>double-blind<br>Europe, Israel               |
| <b>diltiazem vs diuretic and/or beta-blocker</b>  |  |  |   |
| NORDIL (diabetic subgroup) , 2000<br>n=351/376<br>follow-up: 4.5 y                            | Diltiazem 180/360 mg diltiazem daily at step one<br>versus<br>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<br>open<br>Norway, Sweden                       |
| <b>calcium-channel blocker vs diuretic or beta-blocker</b>                                    |  |  |   |
| STOP-2 (CCB, diabetic subgroup) , 2000<br>n=231/253<br>follow-up: 5.03y                       | Calcium-channel blocker<br>versus<br>diuretic or beta-blocker  | diabetic (subgroup) elderly patients aged 70-84 years  | Parallel groups<br>open with blind assessment<br>Sweden         |
| <b>felodipine or isradipine vs diuretic or beta-blocker</b>                                   |  |  |   |
| STOP-2 (CCB vs diuretic or beta-blocker) , 1999<br>n=2196/2213<br>follow-up: up to 6 years    | felodipine 25 mg or isradipine 25 mg daily<br>versus<br>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<br>Open   |
| <b>nisoldipine vs enalapril</b>   |  |  |   |

continued...

| <b>Trial</b>   | <b>Treatments</b>  | <b>Patients</b>  | <b>Trials design and methods</b>        |
|--|--|--|---|
| <b>ABCD (hypertension) , 1998</b><br>n=235/235<br>follow-up: 5 y     | nisoldipine (long acting)<br>versus<br>enalapril   | patients with non-insulin-dependent diabetes<br>and hypertension                                 | Factorial plan<br>Double blind<br>USA   |
| <b>amlodipine vs fosinopril</b>                                      |  |  |   |
| <b>FACET , 1997</b><br>n=191/189<br>follow-up: 3.5 y                 | amlodipine (long acting) 10 mg daily<br>versus<br>fosinopril 20 mg daily   | hypertensive patients with NIDDM   | Parallel groups<br>open<br>Italy        |
| <b>amlodipine vs lisinopril</b>                                      |  |  |   |
| <b>ALLHAT (CCB vs ACEI) , 2002</b><br>n=9048/9054<br>follow-up: 4.9y | Amlodipine 2.5 to 10g/d , Amlodipine 2.5 to<br>10g/d , Amlodipine 2.5 to 10g/d<br>versus<br>lisinopril 10 to 40 mg/d | participants aged 55 years or older with<br>hypertension and at least 1 other CHD risk<br>factor | Parallel groups<br>Double aveugle<br>US |

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## 4 direct renin inhibitor

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

continued...

| Trial  | Treatments  | Patients  | Trials design and methods                       |
|--|---|---|---|
| <b>AVOID , 2008</b><br>[NCT00097955]<br>n=301/298<br>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<br>versus<br>placebo | patients with hypertension and type 2 diabetes with nephropathy | Parallel groups<br>double blind<br>15 countries |

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### AVOID, 2008:

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## 5 diuretics

| Trial  | Treatments   | Patients   | Trials design and methods       |
|--|--|--|---------------------------------|
| <b>chlorthalidone vs placebo</b>   |  |  |                                 |
| <b>SHEP (diabetic subgroup) , 1996</b><br>n=283/300<br>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<br>versus<br>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<br>double-blind |

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## 6 intensive treatment

| Trial   | Treatments  | Patients  | Trials design and methods                       |
|---|---|---|---|
| <b>intensive vs usual</b>   |   |   |   |
| <b>ACCORD (blood pressure) , 2010</b><br>[NCT00000620]<br>n=2363/2371<br>follow-up: 4.7 y | intensive blood-pressure control, targeting a systolic pressure of less than 120 mm Hg<br>versus<br>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<br>open<br>United States, Canada |



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## 7 Treatment blood pressure target

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| 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><br>n=237/233<br>follow-up: 5 year   | intensive treatment with a diastolic blood pressure goal of 75 mmHg<br>versus<br>moderate treatment with a diastolic blood pressure goal of 80-89 mmHg              | diabetes patients with DBP >=90 mmHg                                  | Parallel groups<br>open   |
| <b>ABCD target (N) , 2002</b><br>n=237/243<br>follow-up:  | intensive treatment (diastolic blood pressure decrease of 10 mmHg below baseline DBP)<br>versus<br>moderate treatment (diastolic blood pressure goal of 80-89 mmHg) | diabetes patients with diastolic blood pressure between 80 and 89mmHg | Parallel groups<br>open   |

## References

### ABCD target (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]

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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.