



**STRICTLY EMBARGOED UNTIL Wednesday, 6<sup>th</sup> September at 1000 hours (CET)**


**Amlodipine based regimen to lower blood pressure, reduces the risk of new-onset diabetes in hypertensive patients by more than a third**

**Issued on behalf of the Executive Committee of the Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT)**

6<sup>th</sup> September 2006, Barcelona, Spain – A hypertension regimen based on the calcium channel blocker amlodipine has been shown to reduce the risk of new-onset diabetes by 34 percent in people with high blood pressure, compared with a widely used beta-blocker-based antihypertensive regimen, according to findings from the largest study of hypertensive patients ever conducted in Europe (nearly 20,000 patients). The results were presented today at the World Congress of Cardiology in Barcelona.

The Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT) compared the regimen of the beta-blocker atenolol  $\pm$  the diuretic bendroflumethiazide or the regimen of the calcium-channel blocker, amlodipine  $\pm$  the angiotensin-converting enzyme (ACE) inhibitor perindopril for control of hypertension. 19,257 patients who enrolled in the study, 14,120 did not have diabetes at the outset and 1,366 of these patients developed diabetes over the study period: 567 (8%) in the amlodipine arm and 799 (11.4%) in the atenolol arm.

"One of the most important risk factors for developing new-onset diabetes was being allocated to the beta-blocker  $\pm$  diuretic treatment strategy," Dr Ajay Gupta of the International Centre for Circulatory Health, Imperial College London, UK, said. "Patients allocated to the more modern blood pressure-lowering strategy – amlodipine  $\pm$  perindopril – were 34 percent less likely to develop diabetes. This is important as diabetes significantly increases the risk of myocardial infarctions (heart attacks) and strokes."

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Additionally, the ASCOT study showed that patients who received the beta-blocker based regimen were at increased risk of new-onset diabetes irrespective of all other diabetes risk factors, e.g. increased weight, blood glucose at study entry and initial blood pressure level.

Commenting on the results, Professor Neil Poulter, a member of the Executive Committee of the ASCOT study, said: “These findings have critically important implications for many thousands of people. Hypertension already increases the risk of diabetes 2-3 times. Now we know that the commonly used combination of a beta-blocker ± diuretic significantly increases the risk compared with a new combination, amlodipine ± perindopril. Physicians should think carefully before using the beta-blocker based strategy to treat hypertension.”

Results of the five-year ASCOT trial showed that patients on the amlodipine based regimen experienced an 11 percent reduction in total mortality, a 23 percent reduction in fatal and non-fatal strokes and a 24 percent reduction in cardiovascular death, compared with patients taking the beta-blocker-based regimen. In addition, they had a 10 percent reduction in the primary endpoint of fatal coronary heart disease and non-fatal heart attack, which did not reach statistical significance as the study was halted early due to the mortality benefit associated with the amlodipine based regimen.

A number of independent organisations, such as the UK National Institute for Health and Clinical Excellence (NICE), working with the British Hypertension Society, have recommended that beta-blockers should no longer be the preferred initial therapy for hypertension, and that a calcium-channel-blocker or thiazide-type diuretic should be the first choice for initial therapy in hypertensive patients ages 55 or over, or in black patients of any age. If therapy is initiated with a beta-blocker and a second drug is required, a calcium-channel-blocker should be added rather than a thiazide-type diuretic to reduce the patient’s risk of developing diabetes.<sup>3</sup>



“This data highlights the additional risk of new onset diabetes with a beta-blocker ± diuretic and provides support for this recommendation,” Professor Poulter said.

#### **References**

1. Gupta AK on behalf of the ASCOT investigators. Determinants of new onset diabetes using hypertension patients questioned in the ASCOT-BPLA Trial, World Congress of Cardiology, Barcelona, 6<sup>th</sup> September 2006.
2. Dahlöf B, Sever PS, Poulter NR, Wedel H *et al.* 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;**366**:895-906.
3. NICE Clinical Guideline 34. Hypertension: Management of hypertension in adults in primary care, June 2006.

#### **Note to editors**

Funded by Pfizer, ASCOT was an investigator-led trial coordinated by an independent steering committee. The study began in 1998 and enrolled more than 19,000 patients in the United Kingdom, Ireland, Sweden, Norway, Denmark, Finland, and Iceland. In November 2004, the ASCOT steering committee endorsed the recommendation of the Data and Safety Monitoring Board to stop the trial early due to benefits including mortality, demonstrated in patients who received the calcium-channel-blocker-based regimen.

In ASCOT, all patients had hypertension and at least three pre-specified cardiovascular risk factors such as being ≥55 years old, a smoker and having a family history of coronary events. The aim of the ASCOT trial was to test the hypothesis that calcium-channel-blocker-based antihypertensive treatment regimen is more effective than a beta-blocker-based antihypertensive regimen in the primary prevention of coronary heart disease. The average length of treatment was about 5.5 years.



The early cessation of the study because of the benefits of the amlodipine ± perindopril regimen in the secondary endpoint of all cause mortality meant that there was not enough statistical power for the primary endpoint (non-fatal MI + fatal CHD) to reach statistical significance, although there was a non-significant 10 percent reduction in favour of the amlodipine ± perindopril strategy. The secondary endpoint included all-cause mortality, cardiovascular mortality, fatal and non-fatal stroke, and total coronary events and procedures all of which were significantly reduced by the use of the newer regimen. New onset diabetes was a prespecified tertiary end point.

Norvasc (amlodipine besylate) is indicated for high blood pressure and angina. In clinical trials, the most common side-effects for Norvasc versus placebo were edema (8.3% vs 2.4%), headache (7.3% vs 7.8%), fatigue (4.5% vs 2.8%), and dizziness (3.2% vs 3.4%).

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