



Press release

STRICTLY EMBARGOED UNTIL MONDAY, 4TH DECEMBER 2006 AT 0801 HOURS (GMT)

Risk of heart attack significantly reduced in about 90 days by modern combination of drugs

New results from the only large European study combining blood pressure-lowering with cholesterol reduction in patients with moderate cardiac risk prevents half of heart attacks

London 4th December 2006: The risk of heart attack can be reduced by more than 50 percent by combining a cholesterol-reducing drug, atorvastatin calcium, with a blood pressure-lowering drug, amlodipine besylate, and the benefits are evident for heart attacks as early as 90 days after the start of treatment.

Additionally, in the trial, the simultaneous initiation of atorvastatin and amlodipine treatment was about three times more effective at preventing heart attacks than adding atorvastatin, a statin, to one of the world's most widely used blood pressure-lowering drugs, atenolol, a beta-blocker.

For the first time, results from a large trial – the Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT), which recruited >19,000 patients in the UK, Ireland and the Nordic countries – show that the addition of atorvastatin to amlodipine (a calcium channel blocker) reduced the risk of fatal and non-fatal cardiac events by 53%, and clinical benefits were evident after only three months' treatment ($p=0.02$). This contrasted with the addition of atorvastatin to atenolol, which only achieved a non-significant 16% reduction by the end of the study (median 3.3 years), according to a paper published on-line in the *European Heart Journal* today. (See Figure 1)

According to a principal ASCOT investigator, Professor Peter Sever of the International Centre for Circulatory Health, Imperial College, London, UK, these results have major implications for physicians and their patients worldwide.

“ASCOT demonstrates that the risk of heart attacks can be more than halved in the many patients at moderate risk who doctors see every day. In addition, there is a reduction in strokes of >25 percent. This is achieved by combining two well-known and widely-used drugs – amlodipine and atorvastatin.

“However, if we continue to use older blood pressure-lowering drugs, such as atenolol, and choose only to treat high blood pressure in isolation without giving a statin, we only confer a small part of this potential benefit. As a result, the risk of heart attacks and strokes remains unacceptably high in too many patients despite treatment to blood pressure targets,” Professor Sever said.

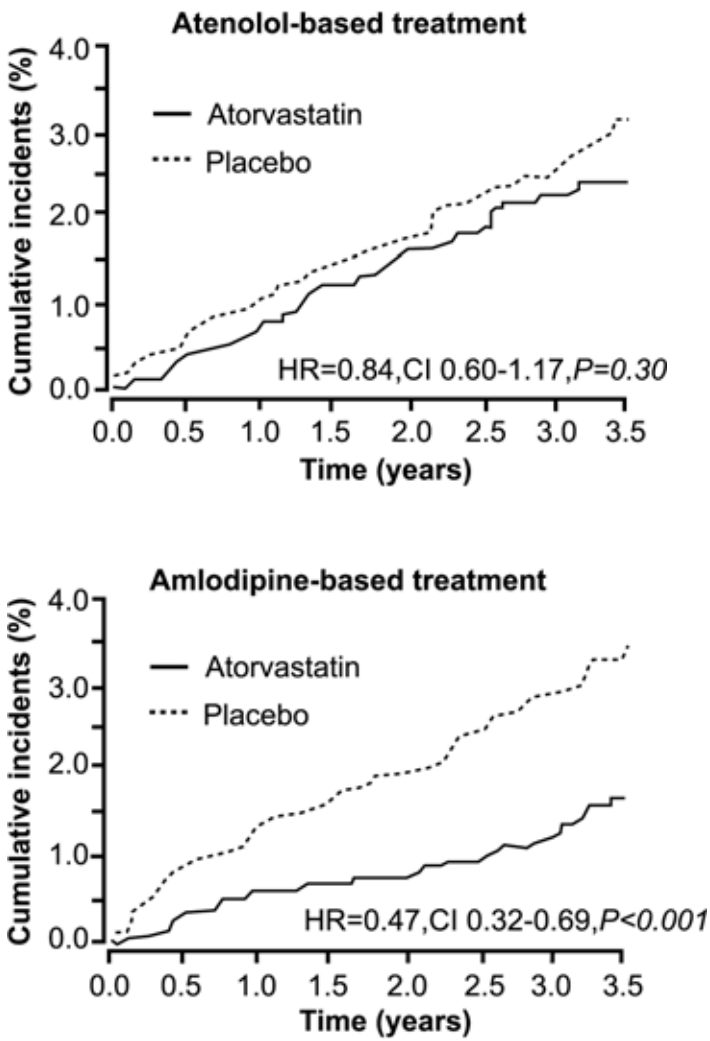


Figure 1. Reducing the risk of heart attacks and coronary disease. Cumulative incidence for non-fatal myocardial infarction (heart attack) and coronary deaths

Results establish important hypothesis for future research

The differences in risk reduction between the two treatments may be explained by recent and ongoing laboratory studies. Earlier laboratory research and clinical studies suggest that amlodipine and atorvastatin may stabilize the fatty deposits in the walls of the arteries (atherosclerotic plaques) which can rupture to cause cardiovascular events such as heart attacks.

Professor Sever said: “The new data generate an important hypothesis that suggests a synergistic effect between atorvastatin calcium and amlodipine besylate, which goes beyond the effects of the individual drugs. This is an exciting possibility for future research, which we and other groups will be exploring.”

The future of treatment

The ASCOT Study is resulting in a re-evaluation of the management of patients with a moderately increased risk of cardiac events worldwide. The importance of combining a contemporary blood pressure drug regimen based on a calcium channel blocker with a statin is gaining importance. Meanwhile, the use of beta-blockers – except where they are specifically indicated – is being questioned.

“For the first time, these important data show that the selection of a blood pressure-lowering drug regimen combined with a statin may have significant clinical implications for preventing heart attacks. It is vital that we use the right combination from the start to maximise the reduction in cardiac risk,” Professor Sever said.

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Note to editors

About cardiovascular risk

More than 330 million adults in Europe and North America suffer from high blood pressure, which also affects an additional 639 million men and women in the rest of the world. (*The Lancet*, January 2005)

About 80% of people with high blood pressure have additional uncontrolled cardiovascular risks. (World Health Organisation).

About ASCOT

ASCOT is the largest European study of people with high blood pressure and ≥ 3 additional common cardiac risk factors, e.g. history of smoking, age > 55 years, diabetes, lipid abnormalities, etc. It included more than 19,000 men and women with high blood pressure who were at a moderate risk of strokes and heart attacks and without previous history of heart disease. To control their blood pressure, they received either the newer drug – a calcium channel blocker, amlodipine besylate – or a beta-blocker, atenolol, to which the ACE inhibitor perindopril or the diuretic bendroflumethiazide were added, respectively, if necessary, to control the BP. Additionally, 10,000 patients also were treated with the cholesterol-lowering drug atorvastatin calcium or a placebo (dummy pill). This is the only major European study to date to combine these two treatment strategies.

The most commonly seen adverse events (AEs) in the amlodipine regimen were peripheral oedema and cough. The most commonly seen AEs in the atenolol regimen were dizziness and fatigue. No new, unexpected AEs were observed beyond those seen in previously published ASCOT results.

Further details can be found at the ASCOT Web site, www.ascotstudy.org

Potential synergy between lipid-lowering and blood pressure-lowering in the Anglo-Scandinavian Cardiac Outcomes Trial Lipid-Lowering Arm

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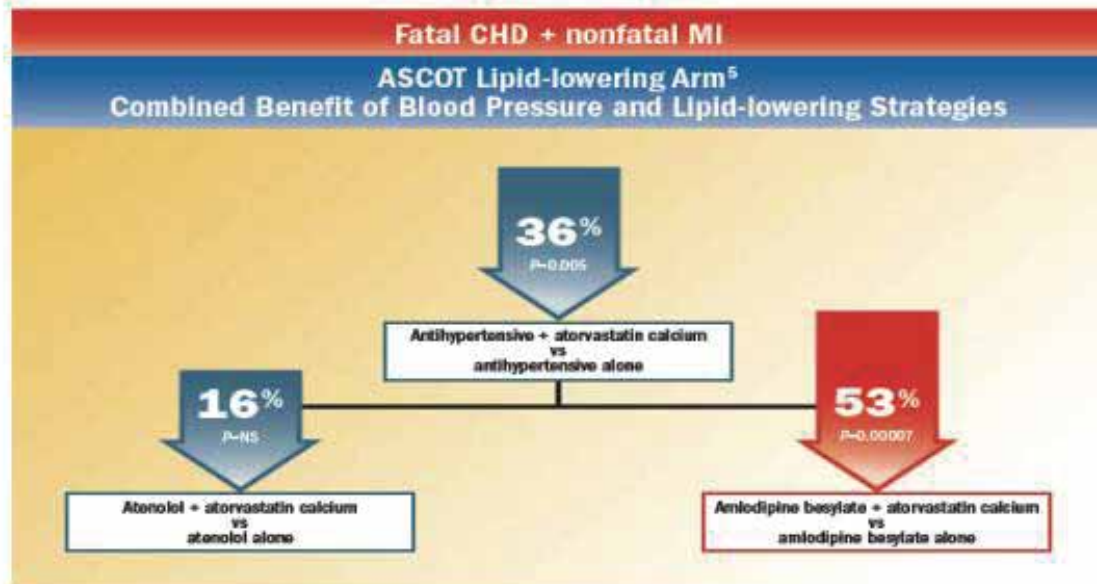
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ASCOT Lipid-lowering Arm assessed the effect of atorvastatin calcium 10 mg versus placebo on fatal and nonfatal CHD in 10,305 treated hypertensive patients without clinically evident CHD and with TC \leq 251 mg/dL. All patients had \geq 3 CV risk factors such as age \geq 55 years, smoking, low HDL-C, or family history of CHD. The primary end point demonstrated a 36% relative risk reduction of nonfatal MI and fatal CHD (P=0.0005). Although the reduction of fatal and nonfatal stroke did not reach a predefined significance level (P=0.01), a favorable trend was observed. All patients were treated with antihypertensive therapy, either amlodipine-based or atenolol-based therapy.^{2,2}

3x Adding atorvastatin calcium to amlodipine besylate is at least 3 times more effective in preventing fatal CHD and nonfatal MI than adding atorvastatin calcium to atenolol.