Cardiovascular trials update

The results of a range of clinical trials were presented at the *45th Annual Scientific Session of the American College of Cardiology*, held in Orlando in March; so much so, that Dr Doug Weaver, Co-chair of the scientific programme committee, described the meeting as "the Woodstock of clinical trials".

Amiodarone safe in myocardial infarction

Two large studies of the Sanofi anti-arrhythmic, amiodarone, confirmed that it was safe to use in post-myocardial infarction (MI) patients and may even reduce mortality in patients at high risk of sudden death.

The European Myocardial Infarct Amiodarone Trial (EMIAT) involved 75 centres in 15 countries. More than 1,400 patients were enrolled immediately following MI and stratified according to their ejection fraction. The study was placebo-controlled and initially a high dose of amiodarone was used (800 mg daily for 14 days, followed by 400 mg for the rest of the first 4 months and then 200 mg daily until the end of the study). Amiodarone produced a significant reduction in secondary end-points, such as arrhythmic death and the combination of resuscitated cardiac arrest and arrhythmic death; the drug had no effect on the primary end-point of total mortality.

In the Canadian Amiodarone Myocardial Infarction Arrhythmia Trial (CAMIAT) study, a lower dose (200 mg daily) was given prophylactically in 21 centres. This was found to reduce the primary end-point of combined arrhythmic death and resuscitated ventricular fibrillation by almost 50%. Favourable trends were also seen in arrhythmic death, cardiac mortality and all-cause mortality. The investigators are now understood to be carrying out sub-group analyses in an attempt to identify groups of patients likely to benefit most from amiodarone treatment.

Increase in pravastatin use likely

Preliminary results of the CARE (Cholesterol and Recurrent Events) study, a 5-year double-blind placebo-controlled study of the cholesterol-lowering drug pravastatin, were given by Dr Eugene Braunwald (Department of Medicine, Brigham and Women's Hospital, Boston, MA, USA). He explained that this was the first trial in patients with normal cholesterol levels following recent heart attack. This is an important group because it is representative of a large number of patients surviving MI.

More than 4,000 men and women who had suffered an MI in the previous 24 months were enrolled. The patients, from 80 centres in the USA and Canada, had an average total cholesterol of 209 mg/dl, similar to that of the US population at large. The risk of subsequent MI was reduced in the pravastatin group by 24% ($P = 0.002$), and these patients were also less likely to require expensive treatment such as coronary artery bypass surgery (26% reduction) and coronary angioplasty (22% reduction). The benefits were particularly clear in women, and it was estimated that for every 1,000 women treated with pravastatin, 248 cardiovascular events, such as MI, were avoided.

Pravastatin was well tolerated, and there was no difference in the overall rate of cancer relative to the placebo group; this is important because questions have been raised about the risk of liver or gastrointestinal cancer in patients treated with pravastatin. This study is likely to change medical practice and to increase the use of pravastatin because it shows that patients with normal cholesterol levels can benefit; all previous studies had concentrated on patients with raised cholesterol.

Abciximab captures attention

Professor Maarten Simoons (Erasmus University, Rotterdam, The Netherlands) presented an interim analysis of CAPTURE data (chimeric 7E3 antiplatelet therapy in unstable angina refractory to standard treatment). CAPTURE is a Phase III, randomized, double-blind, placebo-controlled trial of the antiplatelet agent abciximab (pronounced 'absixymab') in patients requiring urgent percutaneous transluminal coronary angioplasty (PTCA) resulting from refractory unstable angina. The trial was performed in a total of 69 sites in Europe, Israel and Canada.

Normally, patients undergo PTCA soon after admission to hospital, but the CAPTURE results indicate that abciximab given before the operation reduces adverse events, such as MI and death, by 30–50%. Because, on average, about 75% of adverse events occur at the time of PTCA and almost none following it, Professor Simoons claimed "These data indicate there may be a benefit from waiting longer before carrying out PTCA. While this would increase short-term costs, long-term costs would be reduced and the prognosis is better." Originally it was planned to enrol 1,400 patients, but this was halted in December 1995 because of the positive findings described in this interim analysis. Abciximab was developed by Centocor (Malvern, PA, USA) and is now licensed in the USA and Europe for the prevention of acute cardiac ischaemic complications in patients at high risk of abrupt artery closure during angioplasty.

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CombiChem deal

CombiChem (San Diego, CA, USA), the combinatorial chemistry/molecular diversity company founded in 1994, announced its first lead optimization collaboration at the end of April. The partner is Teijin (Osaka, Japan), and the project will focus on the discovery of antagonists to a specific G protein-coupled receptor target. The contract could be worth more than $10 million to CombiChem; the company also retains North and South American rights to commercialize any resulting product.

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