Essential hypertension affects 15–25% of adults in industrial nations and is associated with an increased risk of coronary heart disease (CHD) and cerebrovascular disease – the first and third leading causes of death in the US. Hypertension is estimated to be directly responsible for half of these deaths, and is therefore a major public health issue.

Reducing morbidity and mortality through the prevention and treatment of hypertension represents a major challenge. The introduction of antihypertensive drugs only four decades ago was followed by increased awareness of the condition and their use resulted in improvement in treatment and control rates. However, although age-adjusted mortality rates for stroke and CHD have fallen during this period, rates now appear to be leveling out.

The renin-angiotensin system (RAS) is crucially involved in the development and persistence of elevated blood pressure. Angiotensin II, the final effector molecule of the RAS, plays a particularly important role. As well as increasing blood pressure it has other negative cardiovascular effects – angiotensin II is therefore a prime target for cardiovascular drug therapy. Both the novel angiotensin II receptor blockers (ARBs) and angiotensin-converting enzyme (ACE) inhibitors target the RAS pathway, but only ARBs provide specific RAS blockade selective for the AT1 receptor subtype, through which most of the actions of angiotensin II are mediated. Although the widely used ACE inhibitors, calcium channel blockers, beta-blockers, and diuretics reduce blood pressure in many hypertensive patients, their use is often limited by lack of efficacy, adverse effects, contraindications and poor patient compliance. ARBs have similar hemodynamic effects to ACE inhibitors but are better tolerated.

The role of the ARB valsartan (Diovan®) in the management of hypertension and associated diseases was examined recently in a satellite symposium of the XIII World Congress of Cardiology, held in Rio de Janeiro, Brazil. Valsartan has been found to have at least as good antihypertensive effects as comparator drugs and is effective in all patient populations, irrespective of age, sex, and race. Valsartan has a side-effect profile indistinguishable from that of placebo and a simple pharmacokinetic profile, which should be an advantage in treating patients with renal or hepatic impairment, or the elderly. Valsartan’s action at the AT1 receptor displays insurmountable antagonism, which is associated with a long duration of action.

In hypertensive patients, left ventricular hypertrophy (LVH) is a major independent risk factor for cardiovascular morbidity and mortality, and regression of the condition may be associated with an improvement in prognosis. Professor Petra Thürmann presented the results of an 8-month randomized double-blind clinical trial comparing valsartan with the beta-blocker atenolol, each as monotherapy or in combination with hydrochlorothiazide, in patients with untreated essential hypertension and LVH. The reduction in blood pressure was similar with valsartan and atenolol, but the decrease in left ventricular mass index was more marked in the valsartan group. Professor Thürmann discussed these findings in the context of recently published trials of losartan and irbesartan.
Treatment of heart failure with valsartan was the focus of a presentation by Professor Jay Cohn. The incidence of heart failure is increasing, due to the aging population and a reduction in mortality from acute cardiac events. Although current treatment decreases morbidity and mortality, risks remain unacceptably high. ACE inhibitors control heart failure by decreasing angiotensin, but failure to suppress the RAS completely lessens their beneficial effects. Professor Cohn described the ongoing placebo-controlled randomized Valsartan in Heart Failure Trial (Val-HeFT), which is investigating the effect of adding valsartan to conventional ACE inhibitors in 5,000 heart failure patients. It is hoped that the hemodynamic and hormonal benefits of adding valsartan will translate into improved long-term outcomes.

Another ongoing randomized trial is comparing the long-term effects of valsartan and the third generation calcium channel blocker amlodipine in high-risk hypertensive patients. Professor Stevo Julius explained that the Valsartan Antihypertensive Long-term Use Evaluation (VALUE) trial will test the hypothesis that valsartan is more effective than amlodipine in decreasing cardiovascular events. Fourteen thousand patients with hypertension and one or more disease factors, such as previous myocardial infarction, and/or one or more associated risk factors such as age, diabetes or high cholesterol, will be included. The VALUE trial involves 14,400 patients in 31 countries and enrollment should be complete by September 1999.

The presentations in this supplement confirm that valsartan is a clinically effective agent for the treatment of both hypertension and LVH, and also has great promise in other disease areas. The results of the Val-HeFT and VALUE trials are eagerly awaited.