European Society of Hypertension Meeting

Calcium antagonists save lives in hypertensive patients with additional risk factors: ADALAT INSIGHT trial results

Gothenburg, Sweden, June 2, 2000 – The final results of the landmark INSIGHT Study (International Nifedipine GITS/OROS Study. Intervention as a Goal in Hypertension Treatment) were presented during the Tenth European Meeting on Hypertension here today which establish the place of the calcium antagonist, ADALAT once-daily, as first-line therapy in hypertensive patients with additional risk factors.

INSIGHT is the first double-blind, prospective, randomised study to investigate the benefits of ADALAT once-daily versus diuretic combination therapy, which is the older drug class recommended currently as first-line antihypertensive treatment in international guidelines.

The study showed that ADALAT once-daily is effective against a previous 'gold standard' (diuretics) in reducing cardiovascular morbidity and mortality. The sum of cardiovascular and cerebrovascular morbidity and mortality, and total mortality was 12.1% (ADALAT) and 12.5% (diuretics) (p=ns), respectively. These rates are approximately 50% lower than predicted on the basis of cardiovascular risk profiling (using Framingham data for untreated individuals) and imply a clear benefit to the patients treated.

A member of the INSIGHT International Steering Committee, Professor Giuseppe Mancia of the Department of Internal Medicine, Ospedale San Gerardo, Monza, Italy, commented that "the protective effect was seen in both treatment arms".
Thus Adalat once-daily matches the cardiovascular protection offered by a previous gold-standard.

ADALAT once-daily also showed excellent blood pressure control in line with optimal target values recommended by the World Health Organisation/International Society of Hypertension (WHO/ISH), the sixth report of the US Joint National Committee on prevention, detection, evaluation and treatment of high blood pressure (JNC-VI) and the British Hypertension Society guidelines. A total of 72% of patients taking ADALAT once-daily monotherapy achieved target blood pressure goals and approximately 90% of these were still controlled after approximately four years therapy.

INSIGHT showed superior results to previous hypertension studies such as HOT (Hypertension Optimal Treatment), UKPDS (UK Prospective Diabetes Study) and STOP-2 (Stop Hypertension-2) in terms of controlling blood pressure. Both nifedipine GITS monotherapy and diuretic combination therapy achieved optimal blood pressure control in line with international treatment guidelines in the majority of patients. The mean blood pressure remained close to 138/82 mm Hg throughout the study.

INSIGHT also provided reassuring data on the long-term tolerability and safety of ADALAT once-daily in these hypertensive patients with additional risk factors. Heart rate remained unchanged. The serious adverse event rate was lower in the ADALAT group than in the diuretic combination (25.2% vs 27.8%; $p=0.02$). ADALAT once-daily was also associated with fewer metabolic-endocrine adverse events than diuretics. Thus, the incidence of new-onset diabetes mellitus was significantly lower in the ADALAT once-daily group (4.3% vs 5.6%, $p<0.05$). There

were also fewer cases of electrolyte disturbances (such as hypokalaemia and hyponatraemia), hyperuricaemia, and hypercholesterolaemia in the ADALAT once-daily group ($p<0.01$).

In addition, fewer cases of gout (1.3% vs 2.1%) and of peripheral vascular disease (3.0% vs 5.3%) were observed in the ADALAT once-daily group ($p<0.01$). Renal function, as indicated by estimated glomerular filtration rate (GFR), proved to be more stable in the ADALAT once-daily group (difference in decline in favour of ADALAT group: 2.3 ml/min, $p<0.05$). The study, therefore, confirms the excellent long-term tolerability and safety of ADALAT once-daily.

The patient population studied in INSIGHT is particularly significant as all participants had other cardiovascular risk factors such as diabetes, smoking, hypercholesterolaemia or target organ damage in addition to hypertension. This group of patients is commonly seen in medical practice and provides a realistic clinical trial for these antihypertensive agents.

INSIGHT establishes ADALAT once-daily as the calcium antagonist with the best-documented benefits of long-term outcome in hypertensive patients with additional risk factors. ADALAT once-daily provides excellent blood pressure control and the study confirms the role of ADALAT once-daily as first-line therapy for hypertensive patients with additional risk factors.

The INSIGHT study compared two antihypertensive therapies: the long-acting calcium channel blocker, nifedipine once-daily, and the diuretic combination, hydrochlorothiazide and amiloride, which are the drugs of choice in elderly patients with hypertension. These therapies provide effective 24-hour control of blood pressure

and have high trough-peak ratios. Second and third drugs were given if necessary to allow patients to achieve target blood pressure levels.

INSIGHT was conducted in 703 hospital and general practice centres in eight countries in Europe and in Israel. The study included 6,321 men and women aged 55–80 years with essential hypertension (blood pressure >150/95 mm Hg) or isolated systolic hypertension (systolic blood pressure >160 mm Hg irrespective of diastolic pressure) and one or more additional cardiovascular risk factor.

Leverkusen, June 2, 2000