AstraZeneca

STUDY REPORT SUMMARY

ASTRAZENECA PHARMACEUTICALS

FINISHED PRODUCT: Atacand
ACTIVE INGREDIENT: Candesartan

Study No: NCT0115267
Effects of Angiotensin Converting Enzyme (ACE) Inhibitors Versus Candesartan in Reducing Cardiovascular Events in Primary Treatment of Hypertension (ARBACE)ion

Developmental Phase: Phase IV (database audit study)

Study Completion Date: 15.11.2010 (data base lock)

Date of Report: 10.11.2011

OBJECTIVES:

The primary objective was to investigate the risk of cardiovascular disease (CVD) and new onset diabetes in patients on primary hypertensive treatment with ACEis (angiotensin converting enzyme inhibitors) or candesartan.

Secondary objectives were:

- To investigate the risk of CVD and new onset diabetes in patients on anti-hypertensive treatment with specific types of ACEi compared with candesartan.
- To assess the effect on hypertensive organ damage, renal failure and hyperlipidemia
- To compare the adherence and discontinuation rate between ACEi and candesartan.
- To evaluate differences in use of health care resources, and assess the potential long term cost effectiveness.

METHODS:

Patients prescribed either ACEis or candesartan for hypertension at primary care centers were identified and data was extracted electronically from medical records at 71 primary care centers, and merged with specified national health care registers in Sweden.

Patients with establish CVD and/or malignancy at baseline were excluded. Patients with diabetes at baseline were excluded in the time to diabetes analysis.

Patients were only eligible for the analysis as long as they continued treatment with ACEis or candesartan. The observation period ended on the date when the patient died, started a new renin angiotensin system (RAS) inhibiting drug or until the last valid day of the index prescription.

Statistical methods

Cox regression models were used for CVD risk assessment and the following covariates were used for adjustments: age, gender, diabetes, index year and socio-economic status. More than 85% of the patients prescribed ACEi received enalapril, and all analyses were done with enalapril as comparison in order to reduce potential confounders. Sensitivity analyses were performed with additional adjustment for systolic blood pressure.

The Cox regression model was also used to assess the risk of new onset diabetes.

RESULTS:

Seventy-one primary care centres in Sweden were screened for patients who had been prescribed ACEi or candesartan between the years 1999 and 2007. Among the eligible patients, 22,135 patients were diagnosed with hypertension and prescribed enalapril (n=16,844) or candesartan (n=5,291).

However, due to poorly understood factors, a major difference with respect to calendar time was identified between the two treatment groups. 8,601 of 16,844 patients were started on enalapril during the terminal 12 calendar months of the observation period. No corresponding calendar-time effect was observed for candesartan. As alluded to, the factors behind this surge in enalapril prescription are not known. Consequently, matching or adjusting for these imbalances cannot be done, and further analyses of the data are not justified.