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Prescribing decisions should be made based on the approved package insert in the country of prescription

Sponsor/company:	Sanofi-Aventis	**ClinicalTrials.gov Identifier:**	NA
Generic drug name:	Ramipril	**Study Code:**	HOE498_4099
		Date:	13 Dec 2007

Title of the study and study number:	A multicentre open, non comparative study of the safety of Ramipril (Tritace) 10 mg/day in prevention of cardiovascular events in high-risk patients, following the criteria of the HOPE Study. HOE 498/4099
Investigator(s):	(1)Prof. KMHS Sirajul Haque; (2)Prof. Md. Abu Siddique; (3)Prof. Sajal K Banerjee; (4)Prof. Razia Sultana Mahmud; (5)Prof. Sufia Rahman; (6) Prof. Abdullah Al Shafi Majumder; (7) Prof. Abul Hussain Khan Chowdhury; (8) Prof. Syed Azizul Haque; (9) Dr. Afzalur Rahman; (10) Prof. Mamtaz Hossain; (11) Prof. Abduz Zaher; (12) Prof. AKM Mohibullah;
Study center(s):	(1) Bangabandhu Sheikh Mujib Medical University; (2) Dhaka Medical College & Hospital; (3) National Institute of Cardiovascular Diseases; (4) Sir Salimullah Medical College & Mitford Hospital
Publications (reference):	**Unpublished**

Study period: Date first patient/subject enrolled: 07/10/2003 Date last patient/subject completed: 31/07/2005	**Phase of development:** IV

Objectives:	To investigate the safety of ramipril (Tritace®) 10mg/day used in prevention of cardiovascular events in high-risk patients, including the criteria of the HOPE study.
Methodology:	This multicentre, prospective, open-label, single arm study with ramipril (up to 10mg OAD) was conducted from October 2003 to May 2005. A total of 1012 patients aged 45 years or older at high risk of developing a major cardiovascular event were recruited in the study and assigned to receive ramipril for a period of 2 months.

Number of patients/subjects: Evaluated: 799	Planned: 1000 Efficacy : NA	Randomized: non randomized Safety : Adverse events were observed	Treated : 1012
Diagnosis and criteria for inclusion:	Men and women aged 45 years or older were eligible for the study if they had a history of coronary artery disease, stroke, stable heart failure, peripheral vascular disease, or diabetes with at least one other cardiovascular risk factor (hypertension, elevated total cholesterol levels, low high-density lipoprotein cholesterol levels, cigarette smoking, or documented microalbuminuria).		
Investigational product:	Ramipril (Tritace)		
Dose:	Initial dosage was 2.5mg once daily for 14 days except in patients having stable heart failure. Dosage was increased to 5 mg once daily for 14 more days; if patient compliance was OK, no side effects and abnormal serum creatinine or potassium levels were reported. Then 10 mg (5mg, 2 tablets) once daily was continued as maintenance therapy for 1 month. In patients with stable heart failure (NYHA grade I-III), the starting dose was 1.25mg orally once daily. After 7 days if tolerability was good, the dosage was increased to 2.5mg once daily for 7 more days, then 5mg once daily for 14 days. If the tolerability was still good, dosage was further increased to 10mg once daily and maintained for 1 month. In case of adverse events not allowed to continue the treatment at prescribed dose of ramipril, it was advised to take half of the dose for 2to 3 weeks and then increase the dose at previous level. Titration was continued according to protocol, if patient was compliant to this dosage. If re-increased dose was non-compliant, highest well tolerated one was continued. After the study period, treatment was continued according to the decision of treating physician.		
Administration:	Oral Duration of treatment: 2 months, then treatment following physician's prescription		
Duration of treatment: 2 months	**Duration of observation:** 2 months		
Reference therapy: Dose: Administration:	N/A		
Criteria for evaluation:	The endpoints were the number of discontinuations of treatment (due to adverse events or not), the possibility or not to reach the 10mg/day dose level, the overall number of adverse events, the serious adverse events. No endpoint regarding the efficacy was collected, because the necessary observation time for cardiac events avoidance would have been several years.		
Statistical methods:	Descriptive analysis		

Summary:	During a period of 20 months a total of 1012 patients aged =45 years (mean 57.5 years) who had evidence of vascular disease or diabetes plus one other cardiovascular risk factor or stabilised heart failure (with NYHA grade I to III) were assigned to receive ramipril. Initial dose was 2.5mg once daily which was titrated to 10mg and was maintained for at least 1 month. Finally, 799 patients were evaluated for analysis as they completed treatment as per protocol. Among those 558 (69.8%) patients had reached and continued the dosage of ramipril (Tritace®) 10mg. The incidence of adverse events (AE) was low and reported in 21 (2.6%) patients. The most common AE was cough reported in 12 (1.5%) cases and was possibly related to ramipril. Other adverse events such dizziness, hypotension, headache, weakness were observed in 6 (.08%) patients and was not significant. Only 3 (0.4%) of these patients had to discontinue treatment due to hyperkalemia (2 pts) and increase of serum creatinine (1 pt). 3 (0.4%) patients were died suffering from multiple risk factors and who were enrolled during unstable heart failure. The occurrence of AEs did not seem to be dose-dependent. No endpoint regarding the efficacy was collected, because the necessary observation time for cardiac events avoidance would have been several years.
Date of report:	20/08/2006