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Sponsor/company:	Bristol-Myers Squibb and Sanofi-Aventis	**ClinicalTrials.gov Identifier:**	NCT00265967
		Study Code:	L_9917
Generic drug name:	Irbesartan	**Date:**	03/03 / 2008

Title of the study:	"During NOrmalization of blood pressure, PROBable Leading Even Missing dose" (NO PROBLEM) : A National, Single Center; Single Arr Prospective Clinical Study
Investigator(s):	Prof. Dr.Giray Kabakçi
Study center(s):	Hacettepe University, School of Medicine, Department of Cardiology Ankara, TURKEY
Publications (reference):	None
Study period: Date first **patient** enrolled: **29-SEP-2005** Date last **patient** completed: **29-FEB-2007**	**Phase of development:** Phase IV
Objectives:	Primary Objective: To show the efficacy of irbesartan in regulating diastol blood presure by means of 24 ambulatory blood pressure recording cases of nonadherence to dosage regimen for only one day after treatment period 6-8 weeks with Irbesartan. Secondary Objective: Safety of irbesartan
Methodology:	Patients who meet the inclusion/exclusion criteria and who have bee enrolled in the study received irbesartan treatment for 8 weeks. Irbesarta was initiated at a dose of 150 mg/day to patients were not treated for the hypertention for the last three months before participating to the study. A patients were asked to take their irbesartan treatment on the same hour the day (mornings, 10:00 am.) and record their blood pressures an treatment time (hh:mm) in a patient diary on a daily basis. Patients we evaluated at pre-treatment, at 2-4 weeks of treatment All measuremer were done by patients by using blood pressure manometers provided b the investigators.Irbesartan dosage was increased to 300 mg/day fo patients whom their blood pressures were not effectively controlled after 2 weeks of treatment with irbesartan 150 mg/day. For both dosage group after succesful control is achieved all patients were asked to ceas treatment for one day (protocol specified non-adherence) during weeks 6 8 and Ambulatory Blood Preassure Measuremet (ABPM) was performed.

Number of patients/subjects:	Planned: 80	Randomized: 88	Treated: 64
Evaluated:	Efficacy: 64	Safety: 88	Pharmacokinetics: NA
Diagnosis and criteria for inclusion:	• Hypertensive patients who were over 18 years of age, who hav consented for the study and who were not treated for the last thre months with the following blood pressure levels were enrolled to th study: Mean Diastolic Blood Pressure : = 95 mmHg and = 10 mmHg, or hypertensive patients who had a previous 24 hou ambulatory blood pressure measurement with a diastolic BP of = 8 mmHg. • However, patients with a systolic blood pressure of 180 mmHg (sittin position, screening visit) or with a diastolic BP of =110 mmHg we excluded as well as patients who were diagnosed as secondar hypertension. • Patients with the following initial laboratory results were also exclude - SGPT (ALT) and/or SGOT (ALT)levels 2 times ULN - Serum creatinine: > 2.3 mg/dL (or > 203 µmol/L)		
Investigational product: Dose: Administration:	Irbesartan 150 mg/day (single dose) or 300 mg/day (single dose) Oral		
Duration of treatment: 6 to 8 weeks after the screening visit.	**Duration of observation:** There was no specif observation period assigned within the stud protocol. A one day ambulatory blood pressur control was the main observation of this specifi study.		
Reference therapy: Dose: Administration:	There were no reference treatment/therapies NA NA		
Criteria for evaluation:			
Efficacy:	The efficacy criteria for the study were: • Change in the mean systolic and diastolic blood pressure valu with 24 h ambulatory measurementson the day of compulsor non-adherence to treatment (cessation of treatment for on specified day by the investigators). • Diastolic blood pressure values recorded in patient diaries a well as evaluated during the patient visits .		
Safety:	Adverse events spontaneously reported by the patient and/or noted b the investigators were recorded. For laboratory data, hematology ar blood chemistry which includes serum potassium and tests for live functions were the main parameters for safety. An additional ECG wa performed at each visit.		
Pharmacokinetics:	NA		
Pharmacokinetic sampling times and bioanalytical methods:	NA		

Statistical methods:	Demographical and clinical characteristics of enrolled patients together wi efficacy and safety parameters were evaluated by using descriptiv statistical methods (mean, median, percentage, standard deviation ar confidence intervals). All changes in efficacy parameters as well as su group analysis were be performed by parametric and/or non-parametr tests. Adverse events and occurrence frequencies as well as relationsh with the study treatment were evaluated by using descriptive statistic methods. The significance level was set at $p < 0.05$.
Summary:	
Efficacy results:	Mean diastolic BP was recorded as 97,19 ± 3, 14 mm Hg during th screening visit for patients who have been enrol led to the study (n=88 Mean diastolic BP was decreased to 79 ,63 ± 9, 15 mm Hg during visit (n=76) and to 75,00 + 5,53 mm Hg at Visit 3b (n= 37). Visit 3b was th final visit for the patients whose blood pressure was taken under contr with irbesartan 150 mg treatment and were asked to cease irbesarta treatment for one day and an ambulatory blood pressure measureme was performed. A total of 30 patients whose blood pressure was no effectively controlled were treated with an increased dosage irbesartan (300 mg/day, n=30) and were admitted for ambulatory bloc pressure measurement after their mean systolic blood pressure ha dropped to 76,92 ± 4,80 mm Hg (n=13). Irbesartan either at 150 mg/day or 300 mg/day day effectively controlle the blood pre ssures of recently diagnosed/previously untreated (at lea during the last three months) hypertensive patients. Mean systolic ar diastolic blood pressure values measured by ABPM on the day c missed dose were not different from the previous blood pressure value (Systolic BP; t=1,71, p=0.095; Diastolic BP; t=0,90, p=0.373 for 15 mg/day irbesartan and systolic BP; t=2,01, p=0.068; diastolic BP t=0.290, p=0,776 for 300 mg/day irbesartan). Irbesartan either at 15 mg/day or 300 mg/day effectively controlled the blood pressure fo recently diagnosed and previously untreated hypertensive patien (control rates were 54 % and 77 %, respectively).
Safety results:	During the three routine visits performed for the safety population (n=8 no Serious Adverse Events were recorded. Adverse events were mi and reversible, however in 7 patients overall, severe hypotension (7/8 resulted in cessation of study treatment thus causing withdrawals fro the study. The most common adverse events were increase in ALT ar AST levels during the initial visit (5/88), changes in serum creatinin levels in either direction (6/88) and increase in GGT levels in tw patients. Safety laboratory test changes generally specified as "possibl related with study treatment" by the investigators. Only 76 % of patient had routine ECG evaluations at each visit. ECG evaluations wer regarded as normal. No Serious Adverse Events were reported.
Pharmacokinetic results:	No pharmacokinetic parameters were investigated.
Date of report:	18 Feb 2008