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Sponsor/company:	sanofi-aventis	**ClinicalTrials.gov Identifier:**	NCT00670566
		Study Code:	IRBEH_L_03170
Generic drug name:	Irbesartan / Hydrochlorothiazide	**Date:**	2-Feb-2010

Title of the study:	IrbesartaN/HCTZ to Control Elevated blood pressure to target in moderate to severe hypertensive patieNTs (INCENT study) (Study Number: IRBEH_L_03170)		
Investigator(s):	Prof. Wang Jiguang Ruijin Hospital affiliated to Medical College of Shanghai Jiaotong University		
Study center(s):	20 centers , China		
Publications (reference):			
Study period: Date first patient/subject enrolled: 29-04-2008 Date last patient/subject completed: 18-03-2009		Phase of development: Phase IV	
Objectives:	To evaluate the antihypertensive efficacy of a fixed combination of irbesartan/HCTZ in Chinese moderate to severe essential hypertensive patients		
Methodology:	This is a multi-center, single arm, open label, 12 weeks trial to evaluate the antihypertensive efficacy of a fixed combination of irbesartan/HCTZ in Chinese moderate to severe essential hypertensive patients.		
Number of patients/subjects:	Planned: 500	Randomized: 501	Treated: 501
Evaluated:	Efficacy / Pharmacodynamics: ITT: 501 pts, PP: 449 pts	Safety: 497	Pharmacokinetics: NA
	Efficacy: Intent-to-treat (ITT) Population: 501 patients Per-protocol (PP) Population [patients enrolled according to inclusion /exclusion criteria and completed the 12 weeks treatment]: 449 patients Drop out:47 patients (Reason:AE-13pts, withdrew consent form-18pts, lack of efficacy-5pts, protocol deviation-7pts, other-4pts) Safety population: 497 patients Not taking study medication at all: 4 patients		

Diagnosis and criteria for inclusion:	Enrolled patients aged between 18 to 75 years old with essential hypertension; With blood pressure of 160mmHg≤SeSBP<200mmHg or 100mmHg≤SeDBP<120mmHg for newly diagnosed patients, 140mmHg≤SeSBP<180mmHg or 90mmHg≤SeDBP<110mmHg for uncontrolled monotherapy patients; Willing to discontinue previous antihypertensive medicines prior to entering the study; Written informed consent forms of all patients were obtained.
Investigational product: Dose: Administration:	Irbesartan/HCTZ Newly diagnosed or uncontrolled monotherapy patients[1] → 1 tablet of CoAprovel 150/12.5mg 4weeks → CoAprovel 150/12.5mg + Aprovel 150mg[2] 4weeks → 2 tablets of CoAprovel 150/12.5mg[2] 4weeks follow up at weeks 0, 2, 4, 8 and 12 1. Untreated or treated on monotherapy 2. If BP ≥140/90mmHg for general HTN or ≥130/80 mmHg for HTN with DM Oral
Duration of treatment: 12 Weeks	Duration of observation: 12 weeks after first dose of study medication
Reference therapy: Dose: Administration:	NA
Criteria for evaluation:	
Efficacy: Or Pharmacodynamics:	Efficacy: Primary endpoint: BP control rate at week 12. Secondary endpoint: - Systolic Blood Pressure(SBP) at week 12 vs. baseline; - Diastolic Blood Pressure(DBP) at week 12 vs. baseline; - Proportion of pts. with Microalbuminuria (MAU) at week 12 vs. baseline; - Proportion of pts. with Left Ventricular Hypertrophy(LVH) at week 12 vs. baseline.

Safety:	All adverse events should be recorded in CRF and reported in final study report. All SAEs should be reported according to Chinese regulation and sanofi-aventis' SOPs.
Pharmacokinetics:	NA
Pharmacokinetic sampling times and bioanalytical methods:	NA
Statistical methods:	- Analyze BP control rate at week 12 - Analyze SBP at week 12 vs. baseline; DBP at week 12 vs. baseline; proportion of pts. with MAU at week 12 vs. baseline; proportion of pts. with LVH at week 12 vs. baseline T test, Chi-square test or logrank test were used. All the statistical analyses were done with SAS software (version 9.13).

Summary:

Baseline characteristics*:

	Male (n=237)	Female (n=264)
Age	54.1±9.8	55.9±5.6
Height (cm)	171±5	159±5.2
Weight (kg)	75.8±9.9	64.8±9.1
BMI (kg/m^2)	25.9±3.2	25.6±3.1
SBP (mmHg)	161.5±11.3	163.4±10.0
DBP (mmHg)	99.5±8.6	96.5±8.4
Heart rate (beat/min)	74.7±9.7	74.1±10.1
Hb (g/L)	152±11	134±11
RBC (×10^{12}/L)	4.95±0.44	4.54±0.43
WBC (×10^9/L)	6.65±1.74	6.19±1.45
Blood glucose (mmol/L)	5.67±1.30	5.59±1.18
Serum Creatinine (μmol/L)	82.5±15.2	64.6±16.1
BUN (mmol/L)	5.28±1.37	5.09±1.30
Blood Uric acid (μmol/L)	345.6±68.2	297.3±66.1
AST (U/L)	24.6±9.4	25.0±9.5
ALT (U/L)	27.7±14.9	23.0±12.5
Serum K+ (mmol/L)	4.07±0.37	4.13±0.40
Serum Na+ (mmol/L)	140.9±3.1	141.4±2.7
Serum Cl$^-$ (mmol/L)	103.7±3.3	104.6±3.1

* The baseline data for males and females was similar, with the most notable numerical differences in Hb, serum creatinine and blood uric acid.

Efficacy results:

or

Pharmacodynamic results:

ITT population(n=501):

	Before treatment Baseline	After treatment Week 12	Difference (before and after treatment) (95%CI)
Primary endpoint			
BP control rate (<140/90 mm Hg)	0%	66.1%	66.1%
Secondary endpoint			
SBP (mmHg)	162.5±10.7	134.7±15.0	27.8 *
DBP (mmHg)	97.9±8.6	84.4±9.0	13.5 *
BP control rate ## (<140/90mmHg, Diabetic patients<130/80mm Hg)	0%	57.3%	57.3%

PP population(n=449):

	Before treatment Baseline	After treatment Week 12	Difference (before and after treatment) (95%CI)
Primary endpoint			
BP control rate (<140/90 mm Hg)	0%	72.0%	72.0%
Secondary endpoint			
SBP (mmHg)	162.4±10.7	132.6±13.1	29.9 *
DBP (mmHg)	97.9±8.6	83.5±8.0	14.4 *
MAU,n (%)	150 (33.4)	105 (23.4)	30% #
LVH,n (%) (n=427)	215 (50.4)	175 (41.3)	19% **
BP control rate ## (<140/90mmHg, Diabetic patients<130/80mm Hg)	0%	62.4%	62.4%

*P<0.001; **P=0.01
#P=0.004 ; ## Complementary analysis by principal investigator

Safety results:

A total of 163 adverse events were reported. Adverse events occurring in more than four patients were as following:

AE	Total Patient number n(%)
Dizziness	41(8.1%)
Hyperuricacidemia*	25(4.9%)
Headache	7(1.3%)
Upper respiratory tract infection	6(1.1%)
Hypertension	5(0.9%)
Palpitation	5(0.9%)
Fatigue	5(0.9%)
Transaminase rise **	4(0.7%)

Of 163 adverse events, 4 events were confirmed as serious adverse events.

SAE	Patient number
Cerebral hemorrhage	1
Hypertensive crisis	1
Hypertension-grade 3	1
Lumbar disc protrusion	1

All SAEs are not correlative to study medication.

* Hyperuricacidemia defined as Blood Uric Acid > 420umol/L

**Transaminase rise defined as transaminase rise at week 12 compared to baseline.

Safety results:	

Items	Before treatment	After treatment
Hb (g/L)	142.8±14.4	141.3±15.1
RBC ($\times 10^{12}$/L)	4.74±0.48	4.62±0.49
WBC ($\times 10^{9}$/L)	6.41±1.62	6.42±1.66
Neutrophil (%)	59.3±8.1	59.4±8.0
Lymphocyte (%)	32.5±7.2	32.2±7.1
Blood glucose (mmol/L)	5.64±1.24	5.85±1.59
AST (IU/L)	24.8±9.5	24.6±9.9
ALT (IU/L)	25.3±13.9	26.6±16.3
Creatinine (μmol/L)	73.2±18.0	75.5±18.1
BUN (mmol/L)	5.18±1.33	5.69±1.42
Blood Uric acid (μmol/L)	320.0±71.3	350.0±91.5
K+ (mmol/L)	4.12±0.38	4.14±0.39
Na+ (mmol/L)	141.1±2.91	139.9±2.97
Cl^- (mmol/L)	104.1±3.2	102.9±3.2
Heart rate (beat/min)	74.3±9.9	73.0±8.7

Pharmacokinetic results:	NA
Date of report:	Oct-2009