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Sponsor/company:	sanofi-aventis	**ClinialTrials.gov Identifier:**	NCT00564187
		Study Code:	L_8484
Generic drug name:	Irbesartan	**Date:**	27/Nov/2007

Title of Study: APROVE (Adaptation Posologique, Recherche d'Optimisation et Validation de l'Efficacité tensionnelle): Evaluation of efficacy and safety of the dosage adjustment of Aprovel® (irbesartan) in hypertensive outpatients in current clinical practice

Investigators: Principal Investigator: Pr Habib Haouala, Hôpital Militaire, Tunis

Study centre(s): 23 in Tunisia

Publication (reference): NA

Studied period (years): (date of first enrolment) : 03-feb-2003 (date of last completed) : 05-may-2004	**Phase of development:** IV

Objectives:

Primary : To Evaluate the efficacy of two regimens of irbesartan in patients responding but not normalized at 6 weeks of treatment (schema N°1: maintenance 150mg/day, schema n°2: 300mg/day for 6 more weeks)

Secondary:

- To evaluate the percentage of patients with DBP<90 mmHg at 6 and 12 weeks
- To evaluate the percentage of patients with SBP<140 mmHg at 6 and 12 weeks
- To evaluate rate of adverse events during the study

Methodology: Prospective, multicenter, randomized, open, comparative study.

Evaluation at D0, 6 weeks and 12 weeks.

Randomization of respondent patients not normalized at 6 weeks in two groups (A and B) receiving respectively 150 and 300 mg/day of irbesartan from 6 weeks and 12 weeks.

Number of patients (planned and analysed):

Planned: 150 patients

Included: 115 patients

Analysed ITT: 107 patients

Analysed PP: 66 patients

Diagnosis and main criteria for inclusion: To be included, patients must have the following criteria:

- Mild to Moderate hypertension (90mmHg<DBP<110mmHg and 140mmHg<SBP<180mmHg)
- Or new diagnosed hypertension (after 2 visits within 1 month), never treated before and responding to required conditions for a treatment with irbesartan, after an adapted but insufficient diet
- Or a patient having already been treated with a non-satisfying antihypertensive treatment stopped since at least 2 weeks

before the inclusion

- A minimum exam labs as required by WHO-ISH within the month before the inclusion

Test product, dose and mode of administration:
Irbesartan: 150mg tablets
Dosage: Until 6 weeks: 150 mg/day, then a dosage adjustment according to the blood pressure (normalized: DBP<90mmHg, responding non normalized:DBP=90mmHg and a decrease of DBP=10mmHg, non responding: decrease of DBP<10mmHg and DBP=90mmHg) for the period between 6 and 12 weeks:

- 150 mg/day for normalized patients and patients responding non normalized randomized in the group A
- Or 300 mg/day for non responding patients and responding patients non normalized randomized in the group B

Duration of treatment:
12 weeks

Reference therapy, dose and mode of administration: NA

Criteria for evaluation:
Efficacy:
Number of patients normalized at 12 weeks (DBP<90mmHg)

Safety:
Number of patients having an adverse event, number of patients having a related AE and number of patients having a SAE between D0 and week 12.

Statistical methods:
Descriptive statistics per group: mean, standard deviation, minimum, maximum, median, Q1 and Q3 for continuing data. Number and percentage per group for categorical data.

SUMMARY:

115 patients were included in 23 centers. At week 6, 85 patients were normalized, 8 responding non-normalized and 14 not responding.

The 8 last patients didn't have an evaluation at week 6.

5 normalized patients were not evaluated at week 12.

In Total, 49 patients were excluded from the population per protocol for major deviation from the protocol.

8 patients withdrawn from the study before week 6.

On the 107 patients eligible for the ITT, 41 were excluded from PP.

The mean of age is 54 years, with a predominance of males (57.9%).

23.4% were smoking and 29% had previous cardiovascular disease at D0.

The history of hypertension was at a median of 3.8 months (from 0 to 203 months). 37 from them (34.6%) had already taken an antihypertensive treatment.

At the inclusion, the mean SBP was 162±10mmHg, and DBP 96±6 mmHg.

The mean length of treatment was 12.9±2.8 weeks. During this period, patients took a mean of 93±12 tablets of irbesartan 150, with an observance evaluated at 97.0± 13,1% for the period between D0 and week6, and of 91.2±19,5% for the whole duration of the study.

EFFICACY RESULTS:

The primary criteria of efficacy (percentage of patients normalized at week12 in responding patients non-normalized at week 6) was not correctly evaluated because only 8 patients were concerned, 5 randomized in group A (150 mg/d) and 3 in group B (300 mg/d). 5 patients were normalized in group A at week12 (100.0%) and 1 in group B (33.3%).

We observe a decrease in blood pressure, both diastolic and systolic. This decrease is more important in normalized patients (-18±8 mmHg for DBP at week 12, -32±13 mmHg for SBP at week12) than responding non normalized patients (-16±11 mmHg for SBP at week 12, -18±24mmHg for SBP at week 12) and patient not responding (-11±9 mmHg for DBP at week12, -24±12 mmHg for SBP at week 12).

SAFETY RESULTS:

7 patients (6.3%) had one or more AE between D0 and week 6, and 5 from them (4.5%) were considered as related to the product.

For the period between D0 and week 12, 10 patients had one or more AE, and 5 from them were considered according to the investigators as related to the product.

A SAE was observed (prostate cancer) and estimated non in relation with the product.

Date of the report: 24th November 2005