| | | |
|---|---|---|
| Name of Sponsor/Company: Bristol-Myers Squibb | Individual Study Table Referring to the Dossier | *(For National Authority Use Only)* |
| Name of Finished Product: Aprovel | | |
| Name of Active Ingredient: Irbesartan | | |

# SYNOPSIS

## Full Clinical Study Report for Study CV131-235

**TITLE OF STUDY:** Electrophysiological effects of Irbesartan in patients with paroxysmal AF

**INVESTIGATORS/STUDY CENTERS:**

[redacted]

**PUBLICATIONS:** None

**STUDY PERIOD:** Study Initiation Date: 02-Feb-2006 **CLINICAL PHASE:** PHASE IIIB

Study Completion Date: 28-Jun-2007

**OBJECTIVES:**

*Primary*:

- To compare the mean atrial effective refractory period (AERP) between treatment groups

*Secondary*:

- To assess the effects of irbesartan on the atrial functional refractory period (AFRP)
- To assess the effects of irbesartan on atrial conduction intervals, in subjects with paroxysmal atrial fibrillation (AF)
- To assess the dispersion of refractoriness

**METHODOLOGY:**

Randomized, double blind, placebo controlled, parallel group study.

**NUMBER OF SUBJECTS (Planned and Analyzed):**

44 planned, 14 analyzed.

**DIAGNOSIS AND MAIN CRITERIA FOR INCLUSION:**

Subjects who are going to be admitted (clinical indication out of the protocol) for a catheter ablation for AF.

**TEST PRODUCT, DOSE AND MODE OF ADMINISTRATION, DURATION OF TREATMENT, BATCH NUMBERS:**

Irbesartan 150mg tablets, 150 mg/day orally administered for 1 week, titrated to 300 mg/day orally administered for 1 month if tolerated. Batch no 4G84835.

**REFERENCE THERAPY, DOSE AND MODE OF ADMINISTRATION, DURATION OF TREATMENT, BATCH NUMBERS:**

One placebo tablet orally administered for 1 week, titrated to 2 tablets orally administered for 1 month. Batch no 3A67533.

**CRITERIA FOR EVALUATION:**

**Efficacy:**

*Primary*: AERP

*Secondary*: AFRP, time interval of inter- and intra-atrial conduction, dispersion of refractoriness, and atrial vulnerability (ARR and AF induction)

**Safety:** Adverse events (AEs), clinical laboratory tests results, physical examination, vital signs.

**STATISTICAL CONSIDERATIONS:**

Data were presented as mean ± standard deviation (SD) and compared using Student t-test. A p-value $< 0.05$ was considered statistically significant.

This was an exploratory study and a mean difference of 20-30 milliseconds in AERP between treatment groups was considered meaningful. A sample size of $n = 22$ was calculated assuming an AERP mean difference between the 2 treatment groups of at least 20 milliseconds (SD = 20 milliseconds) to provide 90% or greater power at a 2-sided 0.05 level of significance, considering a loss of 10% of subjects.

**SUMMARY OF RESULTS:**

**Disposition, Demographics, and Other Pertinent Baseline Characteristics:**

Two (2) patients discontinued the study before electrophysiology study (EPS). Twelve (12) patients (5 in the irbesartan arm and 7 in the placebo arm) completed the study. In comparison with the placebo group, the patients in the irbesartan group were younger, weighed more, and had a higher body mass index (BMI). Baseline disease characteristics were similar in both groups.

**Efficacy Results:**

There were no significant differences in AERP between irbesartan and placebo patients (p-values $\geq 0.58$). There were no significant difference in AFRP, inter- and intra-atrial conduction, or atrial vulnerability between irbesartan and placebo patients (p-values $\geq 0.059$).

**Safety Results:**

There were no deaths. There were 4 serious AEs (SAEs) in 2 patients (AF and urinary tract infection in an irbesartan patient and pyrexia and chest pain in a placebo patient). These events were deemed not related to the study therapy by the investigator.

There were 9 AEs in 6/7 irbesartan patients (86%) and 4 AEs in 2/7 placebo patients (29%). All events were mild, except one thrombosis moderate in intensity in the irbesartan group. Three (3) AEs were deemed possibly related to the study therapy by the investigator: a headache in the irbesartan group and a peripheral edema and cardioversion in the placebo group.

**CONCLUSIONS:**

No electrophysiological effect of irbesartan could be demonstrated in patients with paroxysmal AF. Treatment with irbesartan was safe and well tolerated: AEs were mostly mild in intensity and were deemed not related to the irbesartan therapy, except one case of headache.

**DATE OF REPORT:** 01-Oct-2008