Clinical Study Synopsis for Public Disclosure

This clinical study synopsis is provided in line with **Boehringer Ingelheim's *Policy on Transparency and Publication of Clinical Study Data***.

The synopsis - which is part of the clinical study report - had been prepared in accordance with best practice and applicable legal and regulatory requirements at the time of study completion.

The synopsis may include approved and non-approved uses, doses, formulations, treatment regimens and/or age groups; it has not necessarily been submitted to regulatory authorities.

A synopsis is not intended to provide a comprehensive analysis of all data currently available regarding a particular drug. More current information regarding a drug is available in the approved labeling information which may vary from country to country.

Additional information on this study and the drug concerned may be provided upon request based on **Boehringer Ingelheim's *Policy on Transparency and Publication of Clinical Study Data***.

2. SYNOPSIS

Name of company: Boehringer Ingelheim		**Tabulated Study Report**		**(For National Authority Use only)**
Name of finished product: MICARDIS®				
Name of active ingredient: telmisartan		**Page:**	**Number:**	
Ref. To Documentation:	**Volume:**	**Page:** xxx to xxxx		**Addendum No.:**
Report date: 31 August 1999	**Number U99-3144**	**Study period (years):** 30 April 1998 to 08 December 1998		

Title of Study: A Prospective Randomized Open-Label, Blinded-Endpoint (PROBE) Trial Comparing MICARDIS® (telmisartan) (80 mg QD) and Amlodipine (5 mg QD) in Patients with Mild-to-Moderate Hypertension Using Ambulatory Blood Pressure Monitoring

Investigator: Multicentre study without official designation of a Principal or Coordinating Investigator, see section 6 and 16.1.4.

Study center(s): Multicenter. See section 6 and Appendix 16.1.4

Publication (reference): N/A

Clinical phase: IIIb

Objectives: The primary aim of the trial was to demonstrate that telmisartan is superior to amlodipine in lowering ambulatory diastolic and/or systolic blood pressures in the last six hours of the dosing interval. Secondary objectives included evaluations of: 1) the changes from baseline in diastolic and systolic blood pressures during other times during the 24-hr ABPM profile; 2) the changes from baseline in seated trough diastolic and systolic blood pressures as measured by manual cuff sphygmomanometer; 3) responder rates.

Methodology: Prospective randomized open-label blinded-endpoint (PROBE), fixed dose, parallel group comparison trial, using ABPM.

No. of subjects entered:	960 planned
total:	431 randomized
each treatment:	216 telmisartan; 215 amlodipine

Diagnosis and main criteria for inclusion: Mild-to-moderate hypertension defined as the following: a mean seated DBP ≥95 mm Hg and ≤114 mm Hg, a mean seated SBP ≥140 mm Hg and ≤200 mm Hg, and 24-hr mean ABPM blood pressure ≥130/85 mm Hg at the end of a four week placebo run-in period.

Test product:	telmisartan
dose:	80 mg once daily
mode of admin.:	Oral
batch no.:	PD-1840
Duration of treatment:	8 weeks
Reference therapy:	amlodipine
dose:	5 mg once daily
mode of admin.:	oral
batch no.:	commercial product, 8QT027A/8QP028A

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Criteria for evaluation:

Efficacy:
Primary: Changes from baseline in diastolic and systolic blood pressures during the last six hours of the 24-hour dosing interval, as measured by ambulatory blood pressure monitoring (ABPM).
Secondary: Changes from baseline in diastolic and systolic blood pressures during other times during the 24-hr ABPM profile, changes from baseline in seated trough diastolic and systolic blood pressures as measured by manual cuff sphygmomanometer, and responder rates.

Safety: Physical examination, laboratory parameters, 12-lead ECG, blood pressure and pulse rate monitoring and evaluation of adverse events.

Statistical methods: Analysis of covariance; tabulation of adverse events and changes from baseline in ECG, physical exam, and laboratory parameters, summarized by treatment group.

SUMMARY - CONCLUSIONS:

Efficacy results: There were no significant differences found between the effects of telmisartan (Telm) versus amlodipine (amlo) in reducing SBP (-10.4 and –11.1 mm Hg, respectively) or DBP (-6.3 and -6.6 mm Hg, respectively) during the last 6-hours (ABPM) of the dosing interval. Amlo had reductions in SBP/DBP which were 0.7/0.3 mm Hg more than for Telm. Although the goal was to show that Telm reduced blood pressure compared more than amlo, this goal was not met. In fact, the effects of the two treatments were very similar. Statistical evaluations of secondary ABPM endpoints including 24-hour, morning, daytime, nighttime, and blood pressure (SBP and DBP) load, as well as trough cuff blood pressures also found no significant differences between the effects of telm and amlo in the reduction of SBP or DBP. The effects of the two treatments were similar for each of these periods during the 24-hour dosing interval. These statistical findings from the comparisons of the changes from baseline in blood pressure were also confirmed from the blood pressure response variables. For the ABPM results no significant difference was found between the percentage of patients in the two treatment groups identified as being responders relative to SBP (54.7% and 57.8% for Telm and amlo, respectively) or to DBP (39.9% and 35.0% for Telm and amlo, respectively). For the trough cuff results there was an indication ($p=0.02$) that Telm patients were more likely to attain DBP control (DBP <90 mm Hg) than amlo patients (41.9% and 31.3%, respectively). However, this difference between treatments is not found when comparing the percentage of patients in the two treatment groups identified as being responders relative to their trough cuff DBP (51.6% and 47.7% for Telm and amlo, respectively) or their trough cuff SBP (66.1% and 67.3% for Telm and amlo, respectively). Subgroup analyses on the changes from baseline in blood pressure also confirmed the results for all patients. Although the difference between the effects of Telm and amlo on SBP (last 6-hour: -4.9 mm Hg, 24-hour: -5.0 mm Hg, and trough cuff: -4.2 mm Hg) were of a magnitude that could be considered clinically relevant (in favor of amlo), these differences were not statistically significant. There was also an indication that Black patients did not respond to Telm as well as to amlo (differences between treatment effects for SBP: –2.1 and –6.1 mm Hg for 24-hour and trough cuff results respectively, and for DBP:–3.6 and –4.1 mm Hg, respectively). None of the other subgroups (age or gender) indicated any significant (statistical and/or clinical) differences between treatment effects.

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Safety results: The mean duration of drug exposure was comparable (55.2 days) for both drugs. Both Telm and amlo were well tolerated during the eight-week trial, as expected, and most adverse events were mild in severity and transient in nature. The overall percentage of patients with one or more adverse events occurring during the 8-week treatment period was comparable (Telm 44.4% vs. amlo 43.7%), although more events were considered to be drug-related by the investigator in the amlo- treated group (15.8% vs. 8.8%), mostly due to the number of cases of edema which were considered drug-related. Seven (3.2%) Telm and four (1.9%) amlo patients discontinued for adverse events. The overall discontinuation rate during the open-label phase was higher in the t group than in the a group (6.9% vs 3.3%, respectively). There were 12 serious adverse events during the trial, six with an onset post-treatment, none was considered drug-related and only one patient was discontinued due to the SAE. There were a comparable number of new or worsening findings in both treatment groups with regard to physical exams and ECGs, and there were no meaningful changes in laboratory parameters noted, however, marked changes were observed in triglycerides in both treatment groups.

Conclusions: Although superiority of telmisartan versus amolodipine was not observed after eight weeks of treatment, both telmisartan and amlodipine were similar in their ability to reduce blood pressure in mild-to-moderate hypertensive patients, over the course of 24 hours post-dose and were very well tolerated.