Boehringer Ingelheim

Clinical Study Synopsis for Public Disclosure

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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**.

Name of company: Boehringer Ingelheim International GmbH		**Tabulated Study Report**	Boehringer Ingelheim
Name of finished product: Micardis®			
Name of active ingredient: Telmisartan		**Page: 1 of 4**	
Report date: 26 May 2003	**Trial-Number:** 502.376	**Study period (years):** 2001 - 2002	

Title of study:	A prospective, randomised, double-blind, double-dummy trial to compare the efficacy of Micardis® (telmisartan) (80 mg p.o. once daily) and valsartan (160 mg p.o. once daily) in patients with mild-to-moderate hypertension after missing one dose using ambulatory blood pressure monitoring.
Investigators:	[redacted] M.D., Ph.D. [redacted]
Study centres:	43 sites in Europe and South Africa
Publication (reference):	
Clinical phase:	IV
Objectives:	The primary aim of the trial was to demonstrate that telmisartan 80 mg is superior to valsartan 160 mg in lowering diastolic blood pressure in patients who missed a dose of their medication, as measured by ABPM (change from baseline in mean DBP over 24 hours), and that telmisartan 80 mg is superior to valsartan 160 mg in lowering DBP during the last six hours of the dosing interval at the end of a 6 to 8-week treatment period, as measured by ABPM (change from baseline).
Methodology:	Prospective, randomised, double-blind, double-dummy, parallel-group, forced titration, comparison trial, using ABPM
No. of subjects:	
planned:	enrolled: 840 entered:: 420
actual:	enrolled: 849 entered: 440
	Telmisartan: entered: 224 treated: 224 analysed (for primary endpoints): 211/216
	Valsartan: entered: 216 treated: 216 analysed (for primary endpoints): 205/205
Diagnosis and main criteria for inclusion:	Mild-to-moderate hypertension, defined as mean seated DBP of ≥ 95 mmHg and ≤ 109 mmHg and 24-hour mean DBP of ≥ 85 mmHg (as measured by ABPM)
Test product:	Telmisartan (Micardis®)
dose:	40 mg for two weeks, then uptitration to 80 mg, once daily

mode of admin.:	Tablets per os
batch no.:	40 mg: 101997 80 mg: 009640-1
Duration of treatment:	8 weeks
Reference therapies:	1. Valsartan (Diovan®, Kalpress®, Nisis®, Provas swr® , Tareg®, Valpression®, Vals®) 2. Placebo (“missed dose”)
dose:	1. 80 mg for two weeks, then uptitration to 160 mg, once daily 2. One tablet matching telmisartan 80mg/one capsule matching valsartan 160 mg, on day of “missed dose” assessment
mode of admin.:	1. Capsules per os. 2. Tablet/capsule per os
batch no.:	1. 80 mg: B010304 160 mg: B010705 2. Placebo matching telmisartan 80 mg: 101726 Placebo matching valsartan 160 mg: B010704
Criteria for evaluation:	
Efficacy:	Change from baseline in mean DBP measured after a missed dose at the end of a 6 to 8-week treatment period during 24 hours recording (ABPM), and change from baseline in DBP during the last 6 hours of the dosing interval, measured at the end of a 6 to 8-week treatment period by ABPM
Safety:	Evaluation of adverse events and heart rate monitoring
Statistical methods:	Analysis of covariance with baseline as covariate considering centre as main effect

SUMMARY – CONCLUSIONS:

Efficacy results:

After a missed dose, the 24-hour mean DBP was reduced from 92.9 mmHg at baseline by 7.3 mmHg to 85.6 mmHg in the group treated with telmisartan 80 mg. In the group treated with valsartan 160 mg, the 24-hour mean DBP was reduced from 92.7 mmHg by 5.4 mmHg to 87.3 mmHg. The mean difference in DBP change between both treatment groups (adjusted for baseline values and centre) was 1.7 mmHg in favour of telmisartan 80 mg. The advantage of telmisartan 80 mg over valsartan 160 mg in the 24-hour mean DBP after a missed dose is statistically significant (p=0.0061).

The last 6-hour mean DBP after an active dose was reduced from 87.5 mmHg at baseline by 7.1 mmHg to 80.5 mmHg in the group treated with telmisartan 80 mg. In the group treated with valsartan 160 mg the last 6-hour mean DBP was reduced from 86.9 mmHg by 5.9 mmHg to 81.0 mmHg. The difference between both treatments of 0.9 mmHg in favour of telmisartan (adjusted for baseline and centre) is not statistically significant (p=0.2175).

The results regarding SBP are similar to those seen for DBP. The adjusted difference in the 24-hour mean SBP after a missed dose is 2.0 mmHg in favour of telmisartan 80 mg (p=0.0306), and 1.2 mmHg in favour of telmisartan 80 mg (p=0.2305) in the last 6-hour mean SBP after an active dose.

Analysis of secondary endpoints, which reflect mean blood pressure values during other time intervals covered by the ABPMs after a missed and after an active dose of study medication, reveals that differences in favour of telmisartan are greater for time intervals that are more apart from the time of dosing. The advantage of telmisartan 80 mg over valsartan 160 mg is greatest during nighttime and during the last six hours after a missed dose.

Safety results:

The overall incidence of adverse events was comparable between both treatment groups, with slightly lower numbers in the telmisartan group (of 8.5% and 14.5% under telmisartan 40 mg and 80 mg; 11.1% and 17.0% under valsartan 80 mg and 160 mg). There were no SAEs in patients treated with telmisartan, and two with valsartan 160 mg. In the post-treatment period there were three SAEs in two patients who both had been treated with valsartan.

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Conclusions:

Telmisartan 80 mg provides statistically superior 24-h mean ABPM DBP control compared with valsartan 160 mg when a dose was missed. Despite some evidence that telmisartan 80 mg was more favourable than valsartan 160 mg in reducing DBP during the last six hours of the 24-hour dosing interval following an active dose, no significant difference was found.

Differences in favour of telmisartan appear to be greater for time intervals that are farer apart from dosing. The advantage of telmisartan 80 mg over valsartan 160 mg is greatest during nighttime (i.e. 22:00 – 5:59) and during the last six hours after a missed dose.

Telmisartan and valsartan both have a favourable safety profile.