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		**Tabulated Study Report**		
Name of finished product:				
Name of active ingredient: BIRB 796 BS		**Page:**	**Number:**	
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Report date: 28 NOV 2003	**Number:** U03-1713	**Study period (years):** 2001 - 2002		

Title of study:	An open label, randomised, crossover study of the bioavailability of oral BIRB 796 BS tablets (30 mg single dose) with and without administration of oral pantoprazole in healthy male volunteers to assess the effect of gastric pH on absorption of BIRB 796 BS.
Investigator:	[redacted]
Study center:	[redacted]
Publication (reference):	not yet published
Clinical phase:	I
Objectives:	To assess the effect of gastric pH on the pharmacokinetics of BIRB 796 BS. Safety and tolerability were also assessed.
Methodology:	Open label, randomised, single dose crossover study.
No. of subjects:	
planned:	20:
actual:	22 Treatment A: BIRB 796 BS alone entered: 22 treated: 20 analysed (for primary endpoint): 19 Treatment B: pantoprazole then BIRB 796 BS entered: 22 treated: 21 analysed (for primary endpoint): 20
Diagnosis and main criteria for inclusion:	healthy male subjects, age 18 to 55, *Helicobacter pylori* negative
Test product:	BIRB 796 BS + pantoprazole
dose:	BIRB 796 BS 30 mg + pantoprazole 40 mg
mode of admin.:	all medications *per os*
batch no.:	PD-2060, PD 2061, 201681
Duration of treatment:	• BIRB 796 BS single dose in each crossover period • pantoprazole 5 days
Reference therapy:	BIRB 796 BS (no pantoprazole)
dose:	30 mg

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mode of admin.:	*per os*
batch no.:	PD-2060, PD 2061
Criteria for evaluation:	
Efficacy:	primary endpoints: $AUC_{0-\infty}$ secondary endpoints: C_{max}, AUC_{0-t}, t_{max}, CL/F, V_z/F, $t_{1/2}$, MRT, gastric pH measurements
Safety:	secondary endpoints: adverse events; tolerability; vital signs; routine laboratory values, EKG, physical examination
Statistical methods:	PK: bioavailability of BIRB 796 BS with pantoprazole relative to BIRB 796 BS alone based on 90% confidence intervals; correlation between AUC and gastric pH; descriptive statistics Descriptive statistics for safety endpoints and gastric pH measurements.

SUMMARY – CONCLUSIONS:

Efficacy/Pharmacokinetic results:

Using pantoprazole 40 mg once a day for 5 days, the mean gastric pH could be increased from 1.4 to 3.0, a finding similar to other studies in the same population group. . Although all volunteers had an increase in gastric pH the degree of response was variable. The increase in median gastric pH ranged from 0.3 to 3.5 pH units

When BIRB 796 BS tablets were administered in combination with pantoprazole, extent of absorption as measured by $AUC_{0-\infty}$ was equivalent to that of BIRB 796 BS tablets administered alone. The rate of absorption (C_{max}) of BIRB 796 BS was slightly lowered (11%). No apparent differences were found for other pharmacokinetic parameters (AUC_{0-t}, t_{max}, $t_{1/2}$, CL/F, Vz/F and MRT) between the two treatments. Intra-subject variability for BIRB 796 BS tablets was high, 35% for $AUC_{0-\infty}$ and 65% for C_{max}.

Unlike pharmacokinetic parameters, pH parameters showed a consistent effect by pantoprazole. However, there appears to be no clear visual relationships between pharmacokinetic parameters. Correlation analysis showed a weak, albeit significant, negative correlation was found between C_{max} and maximum pH (0-4 hours), C_{max} and pH at drug t_{max}, and C_{max} and pH AUC (0-4 hours). However, only a very small portion of the variation in PK parameters could be accounted for by variation in the pH parameters. No other PK-pH relationships were found.

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Safety results:	There was one sAE in the study, lumboischialgia secondary to a fall 12 days after BIRB 796 BS administration, that was not considered drug related. There was a higher than expected incidence of headache (27%). Of these 6 subjects, 5 had headache within 9 hours of taking BIRB 796 BS and pantoprazole, one had headache within 8 hours of taking BIRB 796 BS alone, and one had headache within 8 hours of taking pantoprazole alone. The cause of the headache is not clear, but the temporal relation to BIRB 796 BS with pantoprazole is present. Pantoprazole 40 mg once daily for 5 days followed by a single dose of 30 mg BIRB 796 BS was well tolerated.
Conclusions:	BIRB 796 BS following pantoprazole was associated with a higher incidence of headache than BIRB 796 BS alone. No consistent effect was observed by pantoprazole in systemic exposure of BIRB 796 BS compared to the control treatment in this crossover study. The extent of absorption for BIRB 796 BS tablets was not altered when co-administered with pantoprazole.