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		**Tabulated Trial Report**	Boehringer Ingelheim
Name of finished product: Not applicable		**EudraCT No.:** 2010-022469-81	
Name of active ingredient: BI 10773		**Page:** 1 of 4	**Synopsis No.:**
Module:		**Volume:** {hyperlink }	
Report date: 01 JUN 2011	**Trial No. / U No.:** 1245.51 / U11-1756-01	**Dates of trial:** 18 NOV 2010 – 20 DEC 2010	**Date of revision:** Not applicable

Title of trial:	Relative bioavailability of 25 mg BI 10773 (Final Formulation) compared to 25 mg BI 10773 XX (Trial Formulation 2) following oral administration in healthy male and female volunteers (an open-label, randomised, single-dose, two-way crossover study)
Principal Investigator:	[redacted]
Trial site:	Human Pharmacology Centre, Boehringer Ingelheim Pharma GmbH & Co. KG, Biberach an der Riss, Germany
Publication (reference):	Data of this study have not been published.
Clinical phase:	I
Objective:	To investigate the relative bioavailability of BI 10773 when administered as 25 mg BI 10773 Final Formulation (FF) compared with 25 mg BI 10773 XX Trial Formulation 2 (TF2)
Methodology:	Open-label, randomised, single-dose, two-way crossover design
No. of subjects:	
planned:	Entered: 24 (at least 8 of each sex)
actual:	Entered: 24 (14 male subjects, 10 female subjects) 25 mg BI 10773 FF: Entered: 24 treated: 22 analysed (for primary endpoint): 21 25 mg BI 10773 XX TF2: Entered: 24 treated: 23 analysed (for primary endpoint): 23
Diagnosis and main criteria for inclusion:	Healthy male and female volunteers, age 18 to 55 years (inclusive), body mass index 18.5 to 29.9 kg/m^2 (inclusive)
Test product:	BI 10773 FF film-coated tablet
dose:	25 mg (single dose)
mode of admin.:	Oral
batch no.:	909473A

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Reference product:	BI 10773 XX TF2 tablet	
dose:	25 mg (single dose)	
mode of admin.:	Oral	
batch no.:	B093000196	
Duration of treatment:	Two single-dose treatments separated by a wash-out period of at least 7 days	
Criteria for evaluation:		
Pharmacokinetics:	Primary endpoints:	$AUC_{0-\infty}$ and C_{max} of BI 10773
	Secondary endpoint:	AUC_{0-tz} of BI 10773
	Other endpoints:	t_{max}, λ_z, $t_{½}$, MRT_{po}, CL/F, and V_z/F of BI 10773
Safety:	Adverse events, vital signs (blood pressure, pulse rate), 12-lead electrocardiogram (ECG), clinical laboratory tests, physical examination, and assessment of global tolerability	
Statistical methods:	Point estimators (geometric means) of the median intra-subject ratios of $AUC_{0-\infty}$, C_{max}, and AUC_{0-tz} and their two-sided 90% confidence intervals were calculated. The statistical model was an analysis of variance (ANOVA) on log-transformed parameters including effects for 'sequence', 'subjects within sequences', 'period', and 'treatment'. Descriptive statistics were calculated for all PK endpoints and for vital signs. Adverse events were analysed using various frequency tabulations.	

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SUMMARY – CONCLUSIONS:

Pharmacokinetics results:

Twenty-four subjects were entered and treated in this trial – 14 males and 10 females ranging in age from 20 to 55 years. Twenty-one subjects completed the trial as planned, 2 subjects disontinued the trial due to adverse events, and 1 subject was excluded due to non-compliance with the protocol.

Following single oral administration of 25 mg BI 10773 XX TF2, BI 10773 was rapidly absorbed, reaching mean peak plasma concentrations at 1.63 h. Thereafter, plasma levels declined in a biphasic fashion with a rapid distribution phase and a slower elimination phase. The mean $AUC_{0-\infty}$ was 5090 nmol·h/L and the mean C_{max} was 764 nmol/L.

Following single oral administration of 25 mg BI 10773 FF, no relevant differences in the rate (C_{max}) and extent ($AUC_{0-\infty}$) of absorption of BI 10773 were observed compared with BI 10773 XX TF2. Mean peak plasma levels of BI 10773 were reached at 1.64 h, the mean $AUC_{0-\infty}$ was 5200 nmol·h/L, and the mean C_{max} was 764 nmol/L.

The geometric mean ratios (90% confidence intervals) of $AUC_{0-\infty}$ and C_{max} were 101.67% (98.10, 105.37) and 99.46% (90.18, 109.68), respectively. Intra-individual variability (% gCV) was 6.7% for $AUC_{0-\infty}$ and 18.7% for C_{max}.

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Safety results:	All 24 subjects entered in this trial were treated: 22 subjects were treated with a single dose of 25 mg BI 10773 FF and 23 subjects were treated with a single dose of 25 mg BI 10773 XX TF2. Treatment-emergent adverse events were reported in 1 subject (4.5%) treated with BI 10773 FF and 7 subjects (30.4%) treated with BI 10773 XX TF2. The most frequently reported adverse event was headache, reported in 1 subject (4.5%) treated with BI 10773 FF and 4 subjects (17.4%) treated with BI 10773 XX TF2. A serious adverse event (severe migraine with aura requiring hospitalisation) was reported in 1 subject treated with BI 10773 XX TF2. As this event occurred 5 days after treatment, the investigator did not consider it related to the study medication. Two subjects were discontinued from the trial due to adverse events occurring after the first treatment – one due to the serious adverse event (migraine) and the other due to nausea, vomiting, and diarrhoea, which also occurred after treatment with BI 10773 XX TF2. The investigator did not consider any adverse events in this trial possibly related to the study medication. Global tolerability was good in all evaluable subjects, and there were no signficant findings in clinical laboratory values, vital signs, or ECG.
Conclusions:	This study demonstrated that the rate and extent of absorption of BI 10773 were similar when administered as the BI 10773 FF compared with BI 10773 XX TF2. The 90% confidence intervals for the geometric mean ratios of both $AUC_{0-\infty}$ and C_{max} were within the standard bioequivalence criteria of 80% to 125%. Following the administration of single doses of BI 10773 FF and BI 10773 XX TF2 to healthy volunteers, tolerability of BI 10773 was good.