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.

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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.:** 2010-022697-14	
Name of active ingredient: BI 135585 XX		**Page:** 1 of 4	**Synopsis No.:**
Module:		**Volume:**	
Report date: 02 SEP 2011	**Trial No. / U No.:** 1283.3 / U11-2244-01	**Dates of trial:** 02 FEB 2011 – 14 MAR 2011	**Date of revision:** Not applicable

Title of trial:	Bioavailability and pharmacokinetics of 50 mg BI 135585 XX administered as tablet with and without food to healthy male 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
Objectives:	To investigate the effect of food on the relative bioavailability of a 50 mg BI 135585 XX tablet
Methodology:	This was an open-label, randomised, single dose, 2-way crossover trial with 2 treatment periods separated by at least 14 days between drug administrations
No. of subjects:	
planned:	entered: 14
actual:	Test treatment (50 mg BI 135585 XX tablet under fed conditions): entered: 14 treated: 14 analysed (for primary endpoint): 14 Reference treatment (50 mg BI 135585 XX tablet under fasted conditions): entered: 14 treated: 14 analysed (for primary endpoint): 14
Diagnosis and main criteria for inclusion:	Healthy male volunteers, age 18 to 55 years inclusive, body mass index 18.5 to 29.9 kg/m^2 inclusive
Test product:	BI 135585 XX jet-milled tablet
dose:	50 mg, single dose
mode of admin.:	Oral, after a high fat, high caloric meal
batch no.:	B101004174

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Reference therapy:	BI 135585 XX jet-milled tablet
dose:	50 mg, single dose
mode of admin.:	Oral, after an overnight fast of at least 10 hours
batch no.:	B101004174
Duration of treatment:	Single dose in each treatment period separated by a wash-out phase of at least 14 days between administrations
Criteria for evaluation:	
Clinical pharmacology:	Primary pharmacokinetic endpoints: $AUC_{0-\infty}$ and C_{max} for BI 135585 XX Secondary pharmacokinetic endpoints: AUC_{0-tz}, $\%AUC_{tz-\infty}$, t_{max}, λ_z, $t_{1/2}$, MRT_{po}, CL/F, and V_z/F for BI 135585 XX
Safety:	Physical examination, vital signs (blood pressure, pulse rate), 12-lead electrocardiogram (ECG), laboratory tests (including hormones of the hypothalamicpituitary-adrenal (HPA) axis and the thyroid gland), adverse events (AEs), and global tolerability assessment
Statistical methods:	Point estimators of the intra-subject ratios (geometric mean ratio; gMean ratio) of the primary endpoints and their two-sided 90% confidence intervals (CIs) were calculated. The statistical model was analysis of variance (ANOVA) on log transformed parameters including effects for 'sequence', 'period', 'treatment', and 'subjects within sequences', the last of which was considered random whereas the others were considered fixed. Descriptive statistics for all other parameters were calculated.

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SUMMARY – CONCLUSIONS:

Clinical pharmacology results:

All 14 healthy male subjects entered in the study completed the 2 treatments as planned. All subjects were white with a mean (range) age of 31.5 (20-48) years and body mass index of 25.76 (22.3-29.6) kg/m^2.

Summary of the selected pharmacokinetic parameters for BI 135585 XX is provided in the table below. When the 50 mg BI 135585 XX jet-milled tablet was administered with food, compared to without food, the exposure to BI 135585 XX ($AUC_{0-\infty}$) was slightly lower and so was the C_{max} value; whereas the t_{max} was slightly higher.

PK Parameter	Fasted (N=14)		Fed (N=14)	
	gMean	gCV%[2]	gMean	gCV%[2]
$AUC_{0-\infty}$ [nmol*h/L]	23100	42.3	21700	35.9
C_{max} [nmol/L]	1140	47.8	1070	32.1
t_{max}[1] [h]	2.75	2.00-5.00	3.50	1.02-5.00

[1] Median and range
[2] Inter-individual variability

Results from the relative bioavailability analysis are summarised in the table below. Both $AUC_{0-\infty}$ and C_{max} met the bioequivalence criteria of 80-125% when 50 mg BI 135585 XX tablet was administered as a single oral dose in the fed state compared to the fasted state.

Parameter	N	Adjust□d gMean ratio [%]	90% CI [%]	gCV [%][1]
$AUC_{0-\infty}$	14	93.70	89.03-98.62	7.6
AUC_{0-tz}	14	93.87	89.28-98.68	7.4
C_{max}	14	93.79	85.12-103.34	14.5

[1] Intra-individual variability

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Safety results: Overall, 4 of the 14 male subjects reported adverse events (AEs) following the administration of single doses of 50 mg BI 135585 XX. One subject had erythema following admnistration of BI 135585 XX under fasted conditions and 4 subjects had 4 AEs (headache, oropharyngeal pain, myalgia from sport, and wound in a finger) following admnistration of BI 135585 XX under fed conditions. No severe AE, investigator-defined drug-related AE, other significant AE, or serious AE occurred. No clinically relevant findings in laboratory evaluation, physical examination, vital signs, or 12-lead ECG were reported. Global tolerability assessment was 'good' for all subjects in both treatments.

Conclusions: Food had no effect with respect to the standard bioequivalence limits of 80-125% on either $AUC_{0-\infty}$ or C_{max} when the 50 mg BI 135585 XX jet-milled tablet was administered as a single oral dose. Moreover, the treatment with or without food was well tolerated. In conclusion, the 50 mg BI 135585 XX jet-milled tablet can be administered with or without food.