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***.

Name of company: Nippon Boehringer Ingelheim		**Tabulated Trial Report**		Boehringer Ingelheim
Name of finished product: Not applicable				
Name of active ingredient: BI 44847		**Page:**	**Number:**	**Synopsis No.:**
Ref. to Documentation:	**Module:**	**Volume:**		
Report date: 27 AUG 2008	**Trial No. / U No.:** 1224.11/ U08-3637-01	**Date of trial:** 3 August 2007 - 25 September 2007		**Date of revision** (if applicable)**:**

Title of trial:	Safety, tolerability, pharmacokinetics and pharmacodynamics of single rising oral doses (50 mg to 800 mg) of BI 44847 as tablet(s) administered to healthy male subjects. A randomised, placebo-controlled (within dose groups) and double-blinded trial.
Principal Investigator:	[redacted]
Trial sites:	[redacted], Japan
Publication (reference):	Data of this study have not been published
Clinical phase:	I
Objectives:	To investigate safety, tolerability, pharmacokinetics and pharmacodynamics of BI 44847 in Japanese healthy volunteers
Methodology:	Randomised, double-blind, placebo controlled within dose groups, single rising dose, single centre
No. of subjects:	48
planned:	entered: 48
actual:	enrolled: 48
	Treatment SRD: entered: 40 treated: 40 analysed (for primary endpoint): 40 Treatment SRD/oGTT: entered: 8 treated: 8 analysed (for primary endpoint): 8
Diagnosis and main criteria for inclusion:	Healthy male volunteers, age ≥20 and ≤35 years, BMI range: ≥18.5 and <25.0 kg/m^2
Test product:	BI 44847
dose:	50 mg, 100 mg, 200 mg, 400 mg and 800 mg
mode of admin.:	having fasted, oral administration with 150 mL of water
batch no.:	BI 44847 50 mg tablet; B06131
	BI 44847 200 mg tablet; B06144

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Reference therapy:	Placebo
dose:	-
mode of admin.:	having fasted, oral administration with 150 mL of water
batch no.:	Matching placebo to BI 44847 50 mg tablet; B06151 Matching placebo to BI 44847 200 mg tablet; B06152
Duration of treatment:	Single dose
Criteria for evaluation:	
Efficacy / clinical pharmacology:	Pharmacokinetic parameters: C_{max}, t_{max}, $AUC_{0-\infty}$, $\%AUC_{tz-\infty}$, AUC_{0-tz}, λ_z, $t_{1/2}$, MRT_{po}, CL/F, V_z/F, Ae_{t1-t2}, fe_{t1-t2}, $CL_{R,t1-t2}$ Pharmacodynamic parameter: glucose in urine Biomarker: plasma glucose
Safety:	Tolerability, adverse events, physical examination, vital signs (BP, PR, body temperature), 12-lead ECG, and laboratory tests
Statistical methods:	Descriptive statistics for safety, PK and PD endpoints will be calculated. Dose proportionality of BI 44847 will be explored using a regression model. A 95% confidence interval for the slope will be computed.

SUMMARY – CONCLUSIONS:

Efficacy / clinical pharmacology results:

Pharmacodynamics and biomarker

Urinary glucose excretion (UGE) in all doses of BI 44847 increased relative to the placebo. The cumulative amount of glucose excreted for 24 hours and 48 hours after dose increased dose-dependently from 50 mg to 800 mg of BI 44847. Most amounts of the UGE were observed within 24 hours after dose.

The plasma glucose profiles of healthy volunteers treated with single doses of BI 44847 from 50 mg to 800 mg were similar to that observed after administration of the placebo. In the 400 mg with oGTT group, plasma glucose concentration after oral glucose intake was suppressed by a single dose of BI 44847.

The difference in $AUEC_{1-5}$ of glucose was statistically significant. This effect on plasma glucose level after oral glucose intake was not observed in 1224.1.

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Efficacy / clinical pharmacology results:	*Pharmacokinetics* BI 44847 was rapidly absorbed following a single oral administration to healthy volunteers. The median t_{max} values ranged from 0.5 to 1 hour. No absorption lag time was observed in this experimental design. Plasma concentrations increased dose-dependently. The increases in C_{max} and AUC in dose groups from 50 mg to 800 mg were slightly over-proportional, in accordance with the findings in 1224.1.
Safety results:	Five subjects (10.4%) experienced AEs during the study, one of whom (2.1%) experienced AEs which was considered by the investigator to be related to the study medication (diarrhoea). All AEs were considered mild in intensity and all subjects recovered from the AEs. No serious adverse events occurred. No subjects died during the study. There were no notable findings of the clinical laboratory evaluation, vital signs, 12-lead ECG, or global tolerability. Single doses of 50 to 800 mg BI 44847 were safe and well tolerated in Japanese healthy male volunteers. The results of this study do not indicate any safety concerns for future clinical trials of BI 44847.
Conclusions:	Single doses of 50 to 800 mg BI 44847 were safe and well tolerated in Japanese healthy male volunteers. The results of this study do not indicate any safety concerns for future clinical trials of BI 44847. Single doses of BI 44847 from 50 mg to 800 mg increased the urinary glucose excretion. A single oral administration of 400 mg of BI 44847 reduced plasma glucose levels in the oGTT. The exposure increased in an over-proportional manner in accordance with increasing dose, and it was much higher than that in the Caucasian trial. There seems to be an ethnic difference in the pharmacokinetics of BI 44847 between Japanese and Caucasians