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: Boehringer Ingelheim		**Tabulated Trial Report**	Boehringer Ingelheim
Name of finished product: Not applicable		**EudraCT No.:** 2008-001460-37	
Name of active ingredient: BI 44370 BS		**Page:** 1 of 3	**Synopsis No.:**
Module:		**Volume:**	
Report date: 30 June 2009	**Trial No. / U No.:** 1246.12 / U09-1595-01	**Dates of trial:** 1 SEP 2008 – 7 NOV 2008	**Date of revision:** Not applicable

Title of trial:	Safety, tolerability and pharmacokinetics of single rising intravenous doses (10 to 50 mg) of BI 44370 BS solution in healthy male volunteers (randomised, single-blind, placebo-controlled within dose groups, Phase I)
Principal Investigator:	[redacted]
Trial site:	Human Pharmacology Centre, Boehringer Ingelheim Pharma GmbH & Co. KG, Ingelheim, Germany
Publication:	Data of this study have not been published.
Clinical phase:	I
Objectives:	To investigate safety, tolerability, and pharmacokinetics of BI 44370 BS solution for intravenous (i.v.) infusion
Methodology:	Randomised, single-blind, placebo controlled within dose groups, single rising dose, single centre
No. of subjects:	
planned:	entered: 24, 8 per dose group (6 on BI 44370 and 2 on placebo)
actual:	entered: 23 BI 44370 entered, treated, and analysed for primary endpoint: 17 Placebo entered, treated, and analysed for primary endpoint: 6
Diagnosis and main criteria for inclusion:	Healthy male volunteers, age 21 to 50 years inclusive, body mass index 18.5 to 29.9 kg/m^2 inclusive
Test product:	BI 44370 solution for infusion 1.0 mg/mL
dose:	10 mg, 25 mg, 50 mg
mode of admin.:	Intravenous
batch no.:	B081002341

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Reference therapy:	Placebo (isotonic sodium chloride solution for infusion 0.9%)
dose:	Not applicable
mode of admin.:	Intravenous
batch no.:	B081002219
Duration of treatment:	One day (single dose, i.v. infusion of 25 min duration)
Criteria for evaluation:	
Clinical pharmacology:	Pharmacokinetic (PK) parameters: C_{max}, t_{max}, $AUC_{0-\infty}$, $\%AUC_{tz-\infty}$, AUC_{0-tz}, $AUC_{t1-t2,}$ AUC_{0-2}, λ_z, $t_{1/2}$, MRT_{inf}, CL, V_z, V_{ss}, Ae_{t1-t2}, fe_{t1-t2}, $CL_{R,t1-t2}$
Safety:	Physical examination, vital signs (blood pressure, pulse rate, respiratory rate, oral body temperature), 12-lead electrocardiogram (ECG), laboratory tests, adverse events (AEs), and assessment of tolerability
Statistical methods:	Descriptive statistics for safety and PK endpoints were calculated. Dose proportionality of BI 44370 BS was explored using a regression model. The 95% confidence interval for the slope was computed.

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SUMMARY – CONCLUSIONS:

Clinical pharmacology results:

Pharmacokinetics

Following i.v. infusion of 10 mg, 25 mg, or 50 mg BI 44370 BS to healthy male volunteers over 25 min, BI 44370 BS followed bi-exponential disposition kinetics. In the dose range investigated, C_{max} and $AUC_{0-\infty}$ increased in proportion with the administered dose. The V_{ss} of BI 44370 BS ranged from 88.3 to 125 L after infusion of 10 mg to 50 mg BI 44370 BS, indicating distribution of the drug into tissue. The clearance of BI 44370 BS was around 1100 mL/min, of which about 13.5% was accounted for by renal excretion of the parent drug. Both CL and CL_R were independent of the dose administered. The $t_{1/2}$ slightly increased with increasing doses from 2.39 h after 10 mg i.v. to 3.48 h after 50 mg i.v., but in general was relatively short. No active substance was measurable in plasma 10 h after infusion of 10 mg and 12 h after infusion of 25 or 50 mg BI 44370 BS. Based on the proportional increase in exposure and the independence of CL from the dose administered, the pharmacokinetics of BI 44370 BS following i.v. infusion can be regarded as linear in the dose range investigated.

Safety results:

After i.v. infusion of single doses of 10, 25, or 50 mg BI 44370 BS or matching placebo to healthy male volunteers, AEs were reported in 3 of the 17 subjects treated with BI 44370 BS and none of the 6 subjects treated with placebo. All 3 subjects with AEs experienced headache. Mild headache was reported in 1 of 6 subjects treated with 10 mg BI 44370 BS i.v. and moderate headache was reported in 2 of 6 subjects treated with 50 mg BI 44370 BS i.v. The investigator considered moderate headache in one of the latter subjects possibly related to the study medication. All AEs were mild to moderate in intensity and all subjects recovered from the AEs. Global tolerability of the study medication was good in all subjects and no clinically relevant laboratory or ECG findings were reported.

Conclusions:

Following i.v. infusion of 10 mg, 25 mg, or 50 mg BI 44370 BS to healthy male volunteers over 25 min, BI 44370 BS exhibited bi-exponential disposition kinetics, tissue distribution, partial renal excretion as parent compound, and linear pharmacokinetics in the dose range investigated.

Single i.v. doses of 10 to 50 mg BI 44370 BS were safe and well tolerated in healthy male volunteers. The results of this study do not indicate any safety concerns for future clinical trials of BI 44370 BS in the dose range investigated.