Boehringer Ingelheim

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 Study Report**	
Name of finished product: N/A			
Name of active ingredient: BI 201335 ZW		**Page:** **Number:**	
Ref. to Documentation:	**Volume: Page:**	**Adde**	**ndum No.:**
Report date: 10 AUG 05	**Number:** U05-1801	**Study period (dates):** 04 OCT 04 - 15 OCT 04	

Title of study:	Safety, tolerance, and pharmacokinetics of single oral doses of 5 mg, 20 mg, 60 mg, 150 mg, 300 mg, 600 mg, 1000 mg, and 1500 mg BI 201335 ZW (PEG 400/TRIS/water solution) in healthy male subjects, in a randomised double blind, placebo controlled rising dose study, followed with an open-label intra-subject two-stage crossover pilot bioavailability comparison of 600 mg BI 201335 ZW in a PEG 400/TRIS/water solution co-administered with food.
Investigator:	[redacted]
Study center(s):	[redacted] [redacted] D-[redacted]
Publication (reference):	N/A
Clinical phase:	l
Objectives:	To assess the safety, tolerance and pharmacokinetics of 5 mg to 1500 mg BI 201335 ZW: 1. In rising single doses 2. Two stage intra-subject bioavailability comparison of 600 mg BI 201335 ZW as a liquid formulation given with and without food.
Methodology:	1. Single rising dose, randomised, placebo controlled, blinded at each dose level 2. Pilot bioavailability comparison: single doses, randomised, intra-individual comparison, open-label.
No. of subjects: **planne d:** **act ual:**	entered: 72; enrolled: 37 (not only for the 5 mg dose group but also for further dose groups which were however not treated) Treatment 5 mg dose group: entered: 8 treated: 8 analysed: 8 Study was discontinued, therefore only the 1st dose group treated;
Diagnosis and main criteria for inclusion:	Healthy male volunteers, age 18 to 55 years
Test product:	BI 201335 ZW in 23mL of 3.1% TRIS: 16.7% water: 80.2% PEG 400 (w:w:w) mixture.

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dose :	administered: 5 mg; planned: 20 mg, 60 mg, 150 mg, 300 mg, 600 mg, 1000 mg, and 1500 mg; only 5 mg administered due to pre-clinical findings
mode of admin.:	p.o.
batch no.:	PEG 400: PD-2516; TRIS: 2512; BI 201335 ZW powder in the bottle: PD-2525 (5 and 20 mg); not administered: PD-2526 (60 and 150 mg), PD-2527 (300, 600, 1000, 1500 and 600 mg);
Duration of treatment:	Single administration
Reference therapy:	Placebo: 3.1% TRIS: 16.7% water: 80.2% PEG 400 (w:w:w)
dose :	0 mg, 1 to 15 mL matching for dose level; however only first dose administered;
mode of admin.:	p.o.
batch no.:	PD-2516 (PEG 400), PD-2512 (PEG 400);
Criteria for evaluation:	
Efficacy:	Pharmacokinetics: plasma concentration time profiles of BI 201335 ZW; PK parameters: C_{max}, $AUC_{0-\infty}$, t_{max}, $t_{1/2}$, CL/F, MRT_{po}, V_z/F; Urine will be collected as planned, but mainly for screening of metabolites and parent drug. The results will be not be part of the CTR.
Safety:	Adverse events; tolerability; vital signs (PR, BP); ECG; physical examination; routine laboratory values.
Statistical methods:	Descriptive statistics
SUMMARY – CONCLUSIONS:	
Efficacy results:	Pharmacokinetics: Mean C_{max} 6 ng/mL, t_{max} 16 h, $AUC_{0-\infty}$ 356 h·ng/mL, $t_{1/2}$ 38 h.
Safety results:	The one administered dose was well tolerated.
Conclusions:	The compound was discontinued because of unexpected pre-clinical findings. The starting dose of 5 mg was well tolerated. Singe 5 mg oral dose of BI 201335 was absorbed very slowly. Systemic exposure was relatively low, but very prolonged and constant. No other conclusions can be drawn as the other planned doses were not administered.