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 Trial Report**	Boehringer Ingelheim
Name of finished product: Not applicable		**EudraCT No.:** Not applicable	
Name of active ingredient: Faldaprevir (BI 201335)		**Page:** 1 of 4	**Synopsis No.:**
Module:		**Volume:**	
Report date: 19 SEP 2014	**Trial No. / U No.:** 1220.52 / c02101188-02	**Dates of trial:** 20 MAR 2013 – 02 MAY 2013	**Date of revision:** Not applicable

Title of trial:	Pharmacokinetics of single and multiple oral doses of 120 mg and 240 mg faldaprevir in healthy Chinese volunteers
Principal Investigator:	[redacted] China
Trial sites:	[redacted] China
Publication (reference):	Data from this trial have not been published at the time of this clinical trial report.
Clinical phase:	I
Objectives:	The objective of this study was to investigate the pharmacokinetics of faldaprevir after single and multiple oral doses (120 mg and 240 mg daily) in Chinese healthy subjects
Methodology:	Randomised, open-label, single and multiple dose design, single-centre study. The study was divided into 2 phases for each dose level (120 mg and 240 mg of faldaprevir): a single dose phase followed by a multiple dose phase. During the single dose treatment (days 1-5), subjects received one single dose in the morning of Day 1. The multiple dose segment started on the morning of Day 6: subjects received multiple oral doses of faldaprevir once daily from Day 6 to Day 15. The duration of the trial was 27 days.
No. of subjects:	
planned:	entered: at least 20
actual:	entered: 25 Treatment 120 mg faldaprevir (treatment 1): single dose phase: entered: 10 treated: 10 analysed (for primary endpoint): 10 multiple dose phase: entered: 10 treated: 10 analysed (for primary endpoint): 10

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actual (continued):	Treatment 240 mg faldaprevir (treatment 2): single dose phase: entered: 15 treated: 15 analysed (for primary endpoint): 13 multiple dose phase: entered: 15 treated: 15 analysed (for primary endpoint): 13
Diagnosis and main criteria for inclusion:	Healthy Chinese male and female subjects, age 18 to 45 years, weight of at least 50 kg, body mass index (BMI) 19 to 24 kg/m^2
Test product:	Faldaprevir (BI 201335) soft gelatine capsule
dose:	Treatment 1: 120 mg (but a loading dose of 240 mg on day 6) Treatment 2: 240 mg (but a loading dose of 480 mg on day 6)
mode of admin.:	Oral
batch no.:	B113000194
Reference therapy:	Not applicable
Duration of treatment:	15 days, comprising 1 single dose on Day 1, 4 days of wash out, and repeated treatment from Day 6 to Day 15.
Criteria for evaluation:	
Clinical pharmacology:	Primary endpoints: $C_{max,ss}$, $AUC_{\tau,ss}$ (after multiple dosing) Secondary endpoints: C_{max}, AUC_{0-tz}, $t_{1/2,ss}$, $t_{max,ss}$ (after single and multiple dosing)
Safety:	Physical examination, vital signs (blood pressure, pulse rate), 12-lead ECG, laboratory tests and adverse events (AEs)
Statistical methods:	Pharmacokinetics and safety were assessed using descriptive analyses only. No interim analyses were conducted.

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SUMMARY – CONCLUSIONS:

Clinical pharmacology results:

A total of 25 subjects were entered in the trial and treated in 2 dose groups, 10 subjects with 120 mg of faldaprevir and 15 subjects with 240 mg of faldaprevir. There were 13 female subjects (52.0%) and 12 male subjects (48.0%). All were Asian, with a mean age of 25.0 years (SD 5.2 years, range 18 to 41 years), and a mean BMI of 21.68 kg/m^2 (SD 1.50 kg/m^2, range 19.0 to 23.8 kg/m^2). No notable imbalances were observed between the dose groups. Three subjects discontinued the trial prematurely due to adverse events.

The results of the primary endpoints are listed below:

Dose	$C_{max,\ ss}$ [ng/mL]	$AUC_{\tau\text{-}ss}$ [ng·h/mL]
120 mg	3270 (44.0)	36200 (48.5)
240 mg	14200 (35.5)	199000 (49.5)

All results are presented as gMean (gCV%)

These results show that $AUC_{\tau,ss}$ and $C_{max,ss}$ increased supra-proportionately with dose: 2-fold increase in dose (from 120 mg to 240 mg) led to a 5.5-fold increase in overall exposure ($AUC_{\tau,ss}$).

The results of the secondary endpoints are listed below:

	Single dosing		Multiple dosing	
	C_{max} [ng/mL]	$AUC_{0\text{-}tz}$ [ng·h/mL]	$t_{1/2,\ ss}$ [h]	$t_{max,\ ss}$ [h]
120 mg	664 (48.7)	14600 (38.9)	31.2 (9.27)	2.99 (1.98 - 4.00)
240 mg	2060 (44.3)	37900 (45.5)	20.0 (23.6)	2.00 (1.98-4.00)

All results are presented as gMean (gCV%), except for $t_{max,\ ss}$ (median and range).

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Clinical pharmacology results (continued):

The results show that C_{max} and $AUC_{0\text{-}tz}$ increased supra-proportionately with dose, and that steady state geometric mean $t_{1/2,ss}$ tended to be longer at lower dose.

Safety results:

In the single dose phase, 7 (70.0%) subjects in the 120 mg dose group and 13 (86.7%) subjects in the 240 mg dose group reported at least 1 AE during the treatment period of the trial. In the multiple dose phase, all subjects reported at least 1 AE. All 25 subjects reported at least 1 AE that was considered by the investigator as related to trial treatment. No AE of severe intensity and no pre-specified AE (i.e. no potential drug-induced liver injury, as specified in the protocol) was reported in this trial. No deaths occurred during the trial.

In the single dose phase, 2 subjects (13.3%) in the 240 mg dose group reported AEs (nausea and vomiting) that led to discontinuation of the trial. In the multiple dose phase, 1 subject (7.7%) from the 240 mg dose group reported AEs (dyspepsia, vomiting, increased conjugated bilirubin, increased blood bilirubin, and increased unconjugated blood bilirubin) that led to discontinuation of trial medication.

There were no notable findings reported as AE with respect to the clinical laboratory evaluation, vital signs, and ECG recordings.

Conclusions:

In Chinese subjects, faldaprevir exposure increased supra-proportionately with dose after a single dose ($AUC_{0\text{-}tz}$, $AUC_{0\text{-}\infty}$, and C_{max}) and at steady state ($AUC_{\tau,ss}$, $C_{max,ss}$) and PK was further time dependent within a dose. This points to a dose dependent non-linear kinetics of faldaprevir in Chinese subjects which is consistent with findings in other populations such as Caucasians. Another consistent finding between Chinese and other populations, female Chinese subjects achieved higher faldaprevir exposure compared to male Chinese subjects.

Overall, the exposure to faldaprevir after multiple doses in Chinese subjects in this trial appeared to be higher than that observed for Caucasian subjects in a previous trial.

From the results of the safety observations, single dose and short-duration multiple dose exposures to 120 mg and 240 mg of faldaprevir were found to be well tolerated in healthy female and male Chinese subjects, in both the single-dose phase and the multiple-dose phase of the trial.