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.

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		**Synopsis**	Boehringer Ingelheim
BI Proprietary Name: Not applicable		**EudraCT No.:** Not applicable	
BI Investigational Product: BI 207127 NA		**Page:** 1 of 5	
Report Date: 26 MAY 2014	**Trial No. / Doc No.:** 1241.22 / c01964084-03	**Dates of Trial:** 09 MAY 2012 – 20 JUN 2012	**Date of Revision:** 13 FEB 2015

Title of trial:	Metabolite profile, excretion balance and pharmacokinetics of BI 207127 NA combined with [^{14}C]-BI 207127 NA in healthy adult male volunteers after an 800 mg single oral solution dose; a phase I, single-arm, open-label trial
Principal Investigator:	[redacted]
Trial site:	[redacted] USA
Publication (reference):	Data from this trial have not been published
Clinical phase:	I
Objectives:	Determination of the pharmacokinetics (PK) and distribution of total radioactivity, including excretion mass balance, and excretion and metabolic pathways following a single oral dose of BI 207127 NA combined with [^{14}C]-BI 207127 NA.
Methodology:	Open-label trial, single oral dose in a single dose group
No. of subjects:	
planned:	entered: 12
actual:	entered: 12 treated: 12 analysed (for primary endpoint): 12
Diagnosis and main criteria for inclusion:	Healthy male volunteers, aged 18 to 55 years (inclusive), body mass index (BMI) 18.5 to 29.9 kg/m^2 (inclusive), nonsmokers for at least 6 months
Test products:	BI 207127 NA (unlabelled powder) combined with [^{14}C]-BI 207127 NA powder in a solution of compendial grade sodium lauryl sulfate, tromethamine, polyethylene glycol 400, and water
dose:	800 mg total: unlabelled BI 207127 NA (minimum of 798 mg) and 100 µCi [^{14}C]-BI 207127 NA (maximum of 2 mg)
mode of admin.:	Oral
batch nos.:	10102 (unlabelled BI 207127 NA); MH-102535-038-1 ([^{14}C]-BI 207127 NA)
Reference therapy:	Not applicable

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Duration of treatment:	Single dose, with an inhouse stay of 6 to 10 days (depending on total radioactive excretion) for PK assessment and biosampling (blood, plasma, saliva, urine, and faeces)
Criteria for evaluation:	
Clinical pharmacology:	Primary endpoints Pharmacokinetics for plasma BI 207127 and [^{14}C]-radioactivity: - $AUC_{0-\infty}$ (area under the concentration-time curve of the analyte in plasma over the time interval from 0 extrapolated to infinity) - C_{max} (maximum measured concentration of the analyte in plasma) - $t_{1/2}$ (terminal half-life of [^{14}C]-radioactivity in plasma) - Excretion balance of total [^{14}C]-radioactivity - Excretion of total [^{14}C]-radioactivity in urine - Excretion of total [^{14}C]-radioactivity in faeces No secondary endpoints were defined for this trial.
Safety:	Safety was assessed as a further endpoint on the basis of physical examination, vital signs (blood pressure, pulse rate, respiratory rate, oral body temperature), 12-lead electrocardiogram (ECG), clinical laboratory tests (haematology, clinical chemistry, and urinalysis), adverse events (AEs), and assessment of tolerability by the investigator
Statistical methods:	Descriptive statistics and graphical displays were employed.

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SUMMARY – CONCLUSIONS:

Clinical pharmacology results:

Of the 12 entered subjects, 8 subjects (66.7%) completed trial assessments as planned; 3 (25.0%) were lost to follow up, and 1 (8.3%) withdrew consent. However, all 12 subjects completed the in-house stay including all planned observations. All 12 treated subjects were male, and 11 subjects (91.7%) were White (information on race was not provided for 1 subject). Mean age was 29.1 years (standard deviation 11.3 years) and mean BMI was 24.7 kg/m^2 (range: 20.3 kg/m^2 to 30.0 kg/m^2).

After oral administration of an 800 mg dose of BI 207127 NA + [^{14}C]-BI 207127 NA, the gMean extent of exposure ($AUC_{0-\infty}$) of BI 207127 was 19300 nmol·h/L, the gMean peak level (C_{max}) was 3620 nmol/L.

Radioactivity from the 100 µCi dose of [^{14}C]-BI 207127 NA was assessed in plasma, whole blood, urine and faeces, and was measured as concentrations (in nmol/L) of [^{14}C]-BI 207127 equivalents (EQ), which should be interpreted as a sum of [^{14}C]-BI 207127 and all metabolites containing the [^{14}C]-label. The [^{14}C]-BI 207127 EQ plasma concentration-time profile was similar to that of BI 207127. Assessment of PK parameters for [^{14}C]-BI 207127 EQ provided a gMean $AUC_{0-\infty}$ of 25800 nmol·h/L, gMean C_{max} of 4280 nmol/L, and gMean $t_{1/2}$ of 2.89 h. Including all 12 subjects, cumulative mean recovery of the radioactive dose was 95.2% (faeces and urine). Geometric Mean fractional urinary excretion of [^{14}C]-BI 207127 EQ was 0.137%, confirming that a very minor proportion of the administered dose of BI 207127 was excreted in the urine either as parent compound or as metabolites. Assessment of faecal excretion of [^{14}C]-BI 207127 EQ demonstrated that by 144 h after administration of [^{14}C]-BI 207127 EQ, 10 of 12 subjects had excreted over 90% of the administered radioactive dose, and that the remaining 2 of 12 subjects had excreted over 80% of the dose. By 168 h, all subjects had excreted at least 91% of the dose. Including all subjects, a geometric mean of 95.1% of the dose was recovered in faeces, indicating that the overwhelming majority of BI 207127 (either as parent compound or as metabolites) was excreted through the faecal pathway (see table below).

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Clinical pharmacology results (continued):

PK parameters of BI 207127 and [^{14}C]-BI 207127 EQ

PK parameter[1]		gMean	gCV [%]
BI 207127			
Plasma			
$AUC_{0-\infty}$	[nmol·h/L]	19300	56.5
C_{max}	[nmol/L]	3620	54.2
[^{14}C]-BI 207127 EQ			
Plasma			
$AUC_{0-\infty}$	[nmol·h/L]	25800	46.1
C_{max}	[nmol/L]	4280	42.3
$t_{1/2}$	[h]	2.89	36.4
Urine			
$f_{e,cum}$	[%]	0.137	37.8
Faeces			
$f_{e,cum}$	[%]	95.1	1.29

[1]N=12

Safety results:

Each of the 12 subjects entered in the trial received a single 800 mg dose of BI 207127 NA, which included 100 µCi [^{14}C]-BI 207127 NA.

Of the 12 subjects entered in the trial, adverse events were reported for 6 (50.0%). By system organ class, gastrointestinal disorders were the most frequently reported adverse events, in 3 of 12 subjects (25.0%), with nausea the most frequently reported preferred term, also in 3 of 12 subjects (25.0%). All adverse events for the trial were of mild intensity. For 4 subjects (33.3%), adverse events were considered drug-related by the investigator; these included dizziness, abdominal discomfort, diarrhoea and nausea in 1 subject, headache and nausea in 1 subject, throat irritation and nausea in 1 subject, and sunburn (on the back) in 1 subject. The sunburn began 294 h (12 days) after administration of trial medication, and resolved after 7 days. No therapy was required. There were no adverse events of severe intensity, prespecified adverse events (drug-induced liver injury), deaths, other serious adverse events, other significant adverse events (as defined by ICH E3), or adverse events leading to discontinuation of the trial drug. All adverse events had resolved by the end of the trial.

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Safety results: (continued)	No relevant mean changes were observed in haematology, coagulation, electrolytes, enzymes, substrates, urine analysis, or inflammatory parameters. One subject had on-treatment decreases in haemoglobin and haematocrit toslightly below the reference range, and 1 subject had on-treatment increases in total and indirect bilirubin to slightly above the reference range. For neither subject were these changes reported as adverse events or considered clinically relevant by the investigator. There were no relevant mean changes in vital signs (blood pressure or pulse rate) or ECG parameters over the course of the trial. No individual change in vital signs or ECG parameters was reported as an adverse event or was considered clinically relevant by the investigator.
Conclusions:	After oral administration of an 800 mg dose of BI 207127 NA + [^{14}C]-BI 207127 NA, the gMean extent of exposure ($AUC_{0-\infty}$) of BI 207127 was 19300 nmol·h/L, the gMean peak level (C_{max}) was 3620 nmol/L. The [^{14}C]-BI 207127 EQ plasma concentration-time profile was similar to that of BI 207127. Geometric mean fractional urinary excretion of [^{14}C]-BI 207127 EQ was only 0.137%. The vast majority of radioactivity (geometric mean of 95.1%) was excreted in the faeces. Administration of a single dose of 800 mg BI 207127 NA, including 100 µCi [^{14}C]-labelled BI 207127 NA, was safe and well-tolerated by the healthy subjects entered in the trial.