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:		**EudraCT No.:** 2005-004005-28	
Name of active ingredient: BI 2536		**Page:** 1 of 4	**Synopsis No.:**
Module:		**Volume:**	
Report date: 26 SEP 2008	**Trial No. / U No.:** 1216.9 / U08-1943-01	**Dates of trial:** 25 JUL 2006 – 01 APR 2008	**Date of revision** (if applicable)**:**

Title of trial:	An open, randomised clinical Phase II trial to investigate the efficacy, safety and pharmacokinetics of a single dose of 200 mg of i.v. BI 2536 in comparison to 50 mg of i.v. BI 2536 administered on days 1, 2 and 3 in patients with advanced or metastatic non small cell lung cancer
Coordinating Investigator:	[redacted]
Trial sites:	Multicentre Study [redacted]
Publication (reference):	Data of this study has been published as abstract (P08-07224).
Clinical phase:	II
Objectives:	To investigate the efficacy, safety and pharmacokinetics of two dosing schedules of BI 2536 in patients with advanced or metastatic non small cell lung cancer and to select the most appropriate dosing schedule for the future clinical trials programme.
Methodology:	Open, randomised, parallel group comparison of two dosing schedules of BI 2536
No. of patients:	
planned:	Entered: 90
actual:	Enrolled: 96 Treatment A (day 1 dosing schedule, 200 mg): Entered: 48 treated: 48 analysed (for primary endpoint): 48 Treatment B/C (day 1, 2 and 3 dosing schedule, [B] 3x50 mg and [C] 3x60 mg): Entered: 47 (B = 26, C = 21) treated: 47 (B = 26, C = 21) analysed (for primary endpoint): 47 (B = 26, C = 21)
Diagnosis and main criteria for inclusion:	Patients with advanced or metastatic non small cell lung cancer (NSCLC) stage IIIB of IV who relapsed after or failed first-line chemotherapy

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Test product:	BI 2536
dose:	Treatment group A: 200 mg on day 1 Treatment group B: 50 mg on days 1, 2 and 3 Treatment group C: 60 mg on days 1, 2 and 3 (after amendment 2)
mode of admin.:	Intravenous (infusion over 60 minutes)
batch no.:	5DB01VAL, 6DB02, 6DB03, 899710
Reference therapy:	Not applicable (n.a.)
dose:	n.a.
mode of admin.:	n.a.
batch no.:	n.a.
Duration of treatment:	1 day or 3 days per treatment course, treatment until withdrawal criteria would be met.
Criteria for evaluation:	
Efficacy / clinical pharmacology:	Objective tumour response was evaluated according to the response evaluation criteria in solid tumours (RECIST), progression free survival (PFS), overall survival (OS), duration of overall response, clinical tumour assessment, quality of life assessment, BI 2536 plasma concentrations.
Safety:	Incidence and intensity of adverse events (AE) graded according to common terminology criteria for adverse events (CTCAE), incidence of dose limiting toxicity (DLT), laboratory investigations and vital signs were assessed.
Statistical methods:	Exact binomial test with 2.5% significance level (one-sided) to detect a difference to historical placebo, exploratory data analysis, confidence intervals (CI) for proportions, Simon's ranking and selection method and Kaplan Meier estimation.

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SUMMARY – CONCLUSIONS:

Efficacy / clinical pharmacology results:

Efficacy:

The results indicate that BI 2536 monotherapy exerts antitumour activity in the treatment of advanced non small cell lung cancer.

Four out of the 95 patients treated had a partial response according to the investigator's judgement (response rate 4.2%) after treatment with BI 2536. Two of them were confirmed by independent review (response rate 2.1%).

The median overall survival was 28.7 weeks (95% CI [25.7, 43.6]) taking both dosing schedules together. The median progression free survival was 58 (95% CI [48, 85]) and 49 (95% CI [46, 70]) days assessed by investigator and independent review, respectively. No statistically significant difference was observed between the two treatment schedules.

There was a moderate trend in improvement for some parameters of quality of life in favour of the day 1, 2 and 3 dosing schedule.

Pharmacokinetics:

The plasma concentration of BI 2536 increased during the infusion period. After the end of infusion BI 2536 showed a fast disposition phase. The plasma concentrations of BI 2535 at 120 hours after the 200 mg dose and 72 hours after the 50 and 60 mg dose were around 2% of those found directly before the end of infusion. The inter-patient variability of the plasma concentrations was moderate after administration of 200 mg (gCV: 37.1-65.5%) and 50 mg or 60 mg (gCV: 30.7- 92.0%) of BI 2536.

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Safety results:	BI 2536 induced reversible neutropenia as expected from the pharmacological profile of the substance. Thirty-seven percent of the patient experienced CTCAE grade 4 neutropenia. On average the nadir was reached 10 days after infusion of the trial drug. Ten patients experienced a fever or infection associated with low neutrophil count. In addition, sepsis and/or febrile neutropenia were reported in one patient each. Fatigue and nausea were the most frequent non haematological adverse events (with maximum of CTCAE grade 3 in two patients each). Forty patients had a serious adverse event under treatment. Out of the 19 patients who died due to a reason other than progressive disease, death was considered drug related by the investigator in two patients (pulmonary haemorrhage and sepsis). BI 2536 is considered to be well tolerated in patients suffering from advanced or metastatic NSCLC.
Conclusions:	This trial provides evidence that Polo-like kinase 1 inhibitors such as BI 2536 may be efficacious in the treatment of non small cell lung cancer.