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:				
Name of active ingredient: BILR 355 BS		**Page:**	**Number:**	
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Report date: 11 April 2006	**Number:** U06-3181	**Study period (dates):** 17 March 2005 to 19 May 2005		

Title of study:	Study of Pharmacokinetic Interaction between TRUVADA™ and BILR 355 BS plus ritonavir
Investigator:	[redacted]
Study center:	[redacted]
Publication (reference):	Data of this study have not been published
Clinical phase:	I
Objectives:	To determine the pharmacokinetic effect of BILR 355 + ritonavir® on TRUVADA and TRUVADA on BILR 355
Methodology:	Open Label, comparative study
No. of subjects:	34
planned:	entered: 34
actual:	enrolled: 79
	Treatment A: entered: 26 treated: 25 analysed (for primary endpoint): Treatment B: entered: 8 treated: 8 analysed (for primary endpoint):
Diagnosis and main criteria for inclusion:	Healthy, HIV negative, adult male and female subjects.
Test product:	BILR 355 BS
dose:	150 mg BID
mode of admin.:	oral
batch no.:	PD 2511 and PD 2421
Duration of treatment:	10-17 days
Reference therapy:	TRUVADA™
dose:	1 tablet QD
mode of admin.:	oral
batch no.:	n/a

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Criteria for evaluation:

Efficacy:	N/A
Safety:	Adverse events, laboratory tests, vital signs and physical examinations
Statistical methods:	AUC and C_{max} were log transformed prior to fitting an ANOVA model. 90% confidence intervals were computed, then back-transformed to the original scale to give the geometric mean and interval estimates for the median ratio (test / reference). TRUVADA administered in combination with BILR 355/r was to be declared pharmacokinetically equivalent to TRUVADA given without BILR 355/r if the 90% confidence intervals for tenofovir disoproxil fumarate (TDF) and emtricitabine (FTC) of the median ratios of AUC_{0-12} and C_{max} were within 80%-125%. In a separate report, data from three other interaction trials will be pooled with that of the current trial to perform a similar test of pharmacokinetic equivalence for BILR 355/r when administered with or without TRUVADA.

SUMMARY – CONCLUSIONS:

Pharmacokinetics results:	Following oral multiple co-administration of BILR 355/r and TRUVADA and TRUVADA alone, the geometric mean ratios (combination vs. TRUVADA alone) of TDF and associated 90% CI were 126.29% (120.53, 132.32), 130.77% (117.33, 145.76), and 131.81% (124.46, 139.59), for AUC0-24,ss, $C_{max,ss}$, and Cp24,ss, respectively. The geometric mean ratios (combination vs. TRUVADA) and 90% CI of FTC, were 160.14% (154.15, 166.36), 127.85% (120.53, 135.62), and 222.67% (205.54, 241.22), for AUC0-24,ss, $C_{max,ss}$, and Cp24,ss, respectively. As the 90% CI for all exposure parameters for TDF and FTC fell outside the upper boundary of the no effect range, it is concluded that co-administration of BILR 355/r with TRUVADA increases TDF and FTC concentrations. The co-administration of BILR 355/r with TRUVADA increases the plasma exposure to TDF and FTC, as measured by $AUC_{0-24h,ss}$, by 26% and 60%, respectively.
Safety results:	Overall, BILR 355 BS was well tolerated in this study, with no subjects discontinuing due to an adverse event and no obvious effect on other measures of safety. There was no evidence of increased risk of TDF or FTC toxicity upon co-administration of TRUVADA with BILR 355/r.

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Conclusions:	In summary, the findings of the present study suggest that co-administration of BILR 355/r with TRUVADA is safe, and support performing further clinical studies of this drug combination in HIV-1 infected patients.