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: BILR 355 BS				
Name of active ingredient: BILR 355 BS		**Page:**	**Number:**	
Ref. to Documentation:	**Volume:**	**Page:**		**Addendum No.:**
Report date: 13 January 2006	**Number:** U06-3018	**Study period (dates):** 13 April 2005 to 27 June 2005		

Title of study:	Study of Pharmacokinetic interaction between Kaletra® (LPV/r) and BILR 355 BS plus ritonavir
Investigator:	[redacted]
Study center:	[redacted]
Publication (reference):	N/A
Clinical phase:	I
Objectives:	To determine the pharmacokinetic effect of BILR 355 BS on Kaletra® and of Kaletra® on BILR 355 BS
Methodology:	Open label, comparative study
No. of subjects:	
planned:	entered: 34
actual:	enrolled: 73 Treatment A: entered: 26 treated: 26 analysed (for primary endpoint): 26 Treatment B: entered: 8 treated: 8 analysed (for primary endpoint): 8
Diagnosis and main criteria for inclusion:	Healthy HIV negative adult male and female subjects
Test product:	BILR 355 BS
dose:	150 mg BID in combination with ritonavir capsules (100 mg QD)
mode of admin.:	Oral
batch no.:	PD 2511
Duration of treatment:	10-24 days
Reference therapy:	Kaletra®
dose:	400 mg lopinivir/100 mg ritonavir, BID
mode of admin.:	Oral
batch no.:	xxx

Name of company: Boehringer Ingelheim		**Tabulated Study Report**		
Name of finished product: BILR 355 BS		**SUPPLEMENTARY SHEET**		
Name of active ingredient: BILR 355 BS		**Page:**	**Number:**	
Ref. to Documentation:	**Volume:**	**Page:** **to**		**Addendum No.:**
Report date: 13 January 2006	**Number:** U06-3018	**Study period (years):** 13 April 2005 to 27 June 2005		

Criteria for evaluation:

Efficacy: Primary Endpoints: Steady-state AUC_{0-12h} and C_{max} for LPV when administered as Kaletra both with and without BILR 355 BS; steady-state AUC_{0-12h} and C_{max} for BILR 355 administered with and without Kaletra, and plasma concentration at 24 hours post-final dose, for BILR 355 BS (and ritonavir). Data from the BILR 355/r group will be combined with data from Trials 1188.7, 1188.9 and 1188.10 in a separate pharmacokinetic report.

Safety: Adverse events, laboratory tests, vital signs and physical examinations

Statistical methods: AUC and C_{max} will be log transformed prior to fitting an ANOVA model. 90% confidence intervals will be computed, then back-transformed to the original scale to give the geometric mean and interval estimates for the median ratio (test/reference).

Kaletra® administered in combination with BILR 355 BS will be declared pharmacokinetically equivalent to Kaletra® given without BILR 355 BS if the 90% confidence intervals for LPV and ritonavir of the median ratios of AUC_{0-12h} and C_{max} are within 80%-125%.

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 administer with or without Kaletra®.

SUMMARY – CONCLUSIONS:

Pharmacokinetics results: Following oral multiple administration, the AUC_{0-12},ss, $C_{max,ss,}$ and $Cp_{12,ss}$ values of LPV for BILR 355 BS + Kaletra® treatment were 88600 h.ng/mL, 9940 g/mL, and 5210 ng/mL respectively; for Kaletra® treatment alone, the values were 88200 h.ng/mL, 9850 ng/mL, and 5190 ng/mL, respectively. The geometric treatment ratios of LPV exposures (combination vs. Kaletra® alone) and the associated 90% confidence interval (CI) were 101.7% (96.05, 107.6), 101.1% (95.34, 107.16), and 104.48% (92.37, 118.18), for $AUC_{0-12,\ ss}$, $C_{max,ss,}$ and $Cp_{12h,ss}$, respectively.

Safety results: The overall adverse event rate was similar among the three treatment regimens in this study, with 88.5%, 75% and 87.5% of subjects in the LPV/r, LPV/r+BILR and BILR/r groups, respectively, experiencing at least one AE. Only 5 subjects experienced AEs that were severe in intensity, 2 subjects in the LPV/r group, 3 in the LPV/r+BILR group and none in the BILR/r group. The number of subjects with investigator defined drug related AEs was lower in the BILR/r group (1 subject, 12.5%) than in the LPV/r and LPV/r+BILR groups (17 subjects, 65.4% and 14 subjects, 58.3%, respectively). Gastrointestinal symptoms and fatigue were the most common treatment related adverse events reported in this study.

Name of company: Boehringer Ingelheim		**Tabulated Study Report**		
Name of finished product: BILR 355 BS		**SUPPLEMENTARY SHEET**		
Name of active ingredient: BILR 355 BS		**Page:**	**Number:**	
Ref. to Documentation:	**Volume:**	**Page: to**		**Addendum No.:**
Report date: 13 January 2006	**Number:** U06-3018	**Study period (years):** 13 April 2005 to 27 June 2005		

Conclusions:

Overall, BILR 355 BS was very well tolerated in this study, with only one subject (in the LPV/r+BILR group) discontinuing due to an adverse event (CK increase) and no obvious effect on other measures of safety.

Following oral multiple administration, the AUC_{0-12},ss, $C_{max,ss,}$ and $Cp_{12,ss}$ values of LPV for BILR 355 BS + Kaletra® treatment were 88600 h.ng/mL, 9940 g/mL, and 5210 ng/mL respectively; for Kaletra® treatment alone, the values were 88200 h.ng/mL, 9850 ng/mL, and 5190 ng/mL, respectively. The geometric treatment ratios of LPV exposures (combination vs. Kaletra® alone) and the associated 90% confidence interval (CI) were 101.7% (96.05, 107.6), 101.1% (95.34, 107.16), and 104.48% (92.37, 118.18), for $AUC_{0-12,\ ss}$, $C_{max,ss,}$ and $Cp_{12h,ss}$, respectively. As the point estimates and the associated 90% CI for all exposure parameters of LPV were completely contained within the no effect region of 80-125%, it is therefore concluded that co-administration of BILR 355 with Kaletra® has no effects on the pharmacokinetics of LPV.