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: Aptivus®		**EudraCT No.:** 2005-005023-33	
Name of active ingredient: Tipranavir		**Page:** 1 of 4	**Synopsis No.:**
Module:		**Volume:** {hyperlink }	
Report date: 28 May 2009	**Trial No. / U No.:** 1182.99 / U09-1451-02	**Date of trial:** 2 Apr 2007 – 8 Oct 2008	**Date of revision:** 8 Jun 2009

Title of trial:	Safety and efficacy study of TIpranavir boosted with low dose ritonavir (TPV/r) 500/200mg BID in antiretroviral treatment experienced HIV positive patients with HCV or HBV Co-INfection, with a pilot evaluation of therapeutic drug monitoring (TDM). An Open-label, multicenter, multinational trial with randomisation to standard of care (SOC) or TDM TPV/r therapy (TICINO) This trial was prematurely discontinued.
Principal/Coordinating Investigators:	[redacted]
Trial sites:	Multicentre Study in Argentina, Brazil, France, Germany, Italy, Spain and United States
Publication (reference):	Data of this study has not been published
Clinical phase:	IIIb
Objectives:	The objective of this study was to assess the safety and efficacy of TPV/r (500 mg/200 mg BID) in ARV therapy experienced HIV-1 infected patients co-infected with HCV or HBV in the presence of an NRTI-based, resistance-driven optimized background regimen. The objective of the TDM pilot evaluation was to determine the potential utility of therapeutic drug monitoring in the use of TPV/r in co-infected patients. With FDA and EMEA agreement, the trial was prematurely discontinued before reaching the target number of patients to be entered due to poor recruitment. For this reason analyzing and reporting data as planned for primary and secondary endpoints have not been performed. No objectives were reached and no conclusion can be drawn from this discontinued study.
Methodology:	All participants were randomised to the TDM pilot evaluation. Patients were randomised to TDM (TPV concentrations reported) or standard of care (no TDM results reported) in a 1:1 ratio, with balance of Hepatitis B and Hepatitis C patients in each arm; at least 15% of patients co-infected with hepatitis B.

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No. of subjects:

planned: entered: 200 (170 HIV/HCV and 30 HIV/HBV)

actual: enrolled:52

Treatment SOC HCV:
entered: 2 treated: 2
Treatment SOC HBV:
entered: 2 treated: 2

Treatment TDM HCV:
entered: 6 treated: 5

Treatment TDM HBV:
entered: 1 treated: 1

Diagnosis and main criteria for inclusion:

Three-class (NRTI, NNRTI, and PI) treatment-experienced (a minimum of 3-months duration for each class) with resistance to more than one PI (on the screening resistance testing). Patients that were NNRTI-naïve patients but who had genotypically documented NNRTI-resistance mutations on past or screening resistance testing would be eligible; CD4+ T lymphocyte count ≥50 cells/µl; HIV-1 VL ≥1000 copies/mL at screening; the ARV study treatment regimen consisted of new TPV/r in combination with an OBR of 2-4 agents of the following: N(t)RTIs (NRTI or NtRTI), enfuvirtide (ENF), and/or, where available, an Expanded Access Program (EAP) investigational agent. In total, patients were to have an ARV study treatment regimen consisting of at least 3 agents (TPV/r and two OBRs); chronic hepatitis C Virus infection demonstrated by HCV-RNA positivity or, Chronic hepatitis B infection demonstrated by anti-HBc-IgG Antibody and HB Surface Antigen positivity; any AIDS defining illness listed in the protocl Appendix 10.3.1 have been accepted as long as was resolved, asymptomatic or stable on treatment for at least 12 weeks before screening (Visit 1); the AIDS defining events listed below were not acceptable History of Progressive Multifocal Leukoencephalopathy (PML), Visceral Kaposi's Sarcoma (KS), and/or any malignancy.

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Test product:	Tipranavir
dose:	SOC arm: Tipranavir 500 mg boosted with ritonavir 200 mg TDM arm: Tipranavir 500 mg boosted with ritonavir 200 mg or Tipranavir 750 mg boosted with ritonavir 200 mg or Tipranavir 500 mg boosted with ritonavir 100 mg or Tipranavir 250 mg boosted with ritonavir 200 mg
mode of admin.:	Oral Administration
batch no.:	Tipranavir B063000257 Ritonavir B063000482, B063000564 and B073000311
Reference therapy:	NA
dose:	
mode of admin.:	
batch no.:	
Duration of treatment:	48 weeks
Criteria for evaluation:	
Efficacy / clinical pharmacology:	Due to the limited number of patients entered in the trial only descriptive statistics have been reported. The protocol endpoints were not analyzed since only one patient completed the planned trial period.
Safety:	Due to the limited number of patients entered in the trial only descriptive statistics have been reported
Statistical methods:	Descriptive statistics.

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SUMMARY – CONCLUSIONS:

Efficacy / clinical pharmacology results:	Since only one patient randomised in the TDM arm was allowed to change the treatment dose, no consideration about TDM benefit have been investigated.
Safety results:	With regards to safety, there were one death and two SAEs observed. Three patients discontinued treatment due to AEs, which included cardiac-respiratory arrest, gastrointestinal disorders, and elevation of ALT and AST. The limited safety data did not alter the safety profile of tipranavir/ritonavir (TPV/r) in adult treatment-experienced patients receiving the medication.
Conclusions:	No efficacy, PK, TDM or safety conclusions are able to be worked out from this trial based on limited data collected in the study.