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: BIRB 796 BS		**Page:**	**Number:**	
Ref. to Documentation:	**Volume:**	**Page:**		**Addendum No.:**
Report date: 30 September 2004	**Number:** U04-1549	**Study period (dates):** 19 May 03 – 07 Jan 04		

Title of study:	A 12 week double-blind, randomized, placebo-controlled trial to investigate efficacy, safety and pharmacokinetics of BIRB 796 BS tablets at doses of 50 and 70 mg administered twice a day in patients with active rheumatoid arthritis who have failed at least one DMARD
Investigator:	39 Rheumatologists
Study center(s):	Multi-national (7 countries), multi-centre (39 centres); Rheumatologists in hospital and practices
Publication (reference):	N/A
Clinical phase:	IIa
Objectives:	To determine the efficacy (including ACR 20 response rate), safety, and pharmacokinetics of BIRB 796 BS as monotherapy in patients with moderate to severe rheumatoid arthritis who have failed at least one DMARD
Methodology:	Randomised, double-blind, placebo-controlled, dose-response, multi-centre, multi-national, parallel
No. of subjects:	
Planned:	Enrolled: 370 Entered: 285 with 95 for each treatment
Actual:	Enrolled: 227 Entered: 170 Treatment A: 50 mg BIRB 796 BS bid Entered: 63 Treated: 62 Analysed (for primary endpoint): none Treatment B: 70 mg BIRB 796 BS bid Entered: 50 Treated: 50 Analysed (for primary endpoint): none Treatment C: Placebo Entered: 57 Treated: 56 Analysed (for primary endpoint) none
Diagnosis and main criteria for inclusion:	RA functional class I-III, men or women aged 18-75 years, failure of at least one DMARD, 2 out of the 3 following: 1) 9/68 tender joints, 2) 9/66 swollen joints, 3) CRP ≥ 1.5 mg/dl or ESR ≥ 28 mm/hr at screening.
Test product:	BIRB 796 BS
Dose:	Twice daily doses 50 or 70 mg, respectively
Mode of admin.:	Oral
Batch no.:	PD-2223 (50 mg), PD-2221 and PD-2223 (70 mg)

Name of company: Boehringer Ingelheim		**Tabulated Study Report**		
Name of finished product:		**SUPPLEMENTARY SHEET**		
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Duration of treatment:	12 weeks
Reference therapy:	Placebo tablets
Dose:	-
Mode of admin.:	oral
Batch no.:	PD-2214 (matching 20 mg tablets) and PD-2216 (matching 50 mg tablets)
Criteria for evaluation:	
Efficacy:	ACR 20/50/70, swollen and tender joint counts, patients assessments of disease activity and pain, physicians assessment of disease activity, CRP, ESR, HAQ, number of drop-outs due to lack of efficacy, DAS 28, ACR-N AUC
Safety:	Adverse events, laboratory evaluations, ECGs, physical exams and vital signs, number of withdrawals due to AEs
Statistical methods:	ANOVA, ANCOVA, Wilcoxon Rank Sum Test, Chi-square Test, logistic regression.

SUMMARY – CONCLUSIONS:

Efficacy results.	None. The trial was terminated early due to safety reasons.
Safety results:	The trial was terminated early after thirteen patients treated with BIRB 796 BS experienced alanine aminotransferase (ALT, previously SGPT) elevations of greater than 3 times of upper limit of normal (ULN). Seven of the patients had ALT peaks of greater than 10 times ULN. All thirteen patients also experienced elevations of aspartate aminotransferase (AST, previously SGOT), gamma-glutamyltransferase (GGT) and lactate dehydrogenase (LDH). All seven patients who had ALT elevations of greater than 10 x ULN, had simultaneously AST elevations with peaks ranging from 6.7 to 10.8 x ULN. None of the patients experienced concomitant signs or symptoms of liver dysfunction. All LFT changes normalized within a few days after discontinuation of treatment. Clinically relevant elevations of bilirubin were not observed. All placebo-treated patients had normal LFTs before, during and after treatment.
Conclusions:	The trial was discontinued as it was concluded that a continuation of the trial imposed an inappropriate risk to the health of the patients that was not balanced by appropriate benefits. Consequently, the further clinical development of BIRB 796 BS in the indication Rheumatoid Arthritis was completely discontinued.