Boehringer Ingelheim

Clinical Study Synopsis for Public Disclosure

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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.

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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: not applicable		**EudraCT No.:** 2005-005368-10	
Name of active ingredient: BIRT 2584 XX		**Page:** Page 1 of 4	**Synopsis No.:**
Module:		**Volume:**	
Report date: 05 JUN 2009	**Trial No. / U No.:** 1206.5 / U09-3386-01	**Date of trial:** 16 JUN 2006 to 09 JUN 2008	**Date of revision** (if applicable): not applicable

Title of trial:	A 12 week double-blind, randomised, placebo-controlled, modified dose-escalation trial to investigate safety, efficacy, and pharmacokinetics of BIRT 2584 XX tablets at doses of 100, 300 and 500 mg administered once daily in patients with moderate to severe psoriasis with a 12 week treatment extension for PASI 50 responders.
Coordinating Investigator:	[redacted]
Trial sites:	Multicentre study, [redacted]
Publication (reference):	Data of this study have not been published
Clinical phase:	IIa/b
Objectives:	To investigate the safety, efficacy (proof of concept) and pharmacokinetics of BIRT 2584 XX tablets given orally at doses of 100, 300 and 500 mg q.d. compared to placebo tablets for the treatment of moderate to severe psoriasis.
Methodology:	Randomised, double-blind, placebo-controlled study, parallel group
No. of subjects:	
planned:	enrolled: 540 entered: 360
actual:	enrolled: 143 entered: 68 (enrollment was prematurely discontinued) Treatment placebo: entered: 17 treated: 17 analysed (for primary endpoint = Visit 8): 3 Treatment 100 mg: entered: 17 treated: 17 analysed (for primary endpoint = Visit 8): 2 Treatment 300 mg: entered: 34 treated: 34 analysed (for primary endpoint = Visit 8): 2

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Diagnosis and main criteria for inclusion:	- Adults with moderate to severe plaque-type psoriasis diagnosed at least 6 months before randomisation, minimum disease severity defined by body surface area (BSA) ≥10%, static Physician Global Assessment (sPGA) score of at least 3 and Psoriasis Area and Severity Index (PASI) score ≥10. - Patients had to be candidates for systemic treatment or phototherapy
Test product:	BIRT 2584 XX
dose:	100 mg, 300 mg and 500 mg q.d.
mode of admin.:	per os, oral tablets
batch no.:	PD-2675 (100 mg); PD-2676 (200 mg)
Reference therapy:	placebo
dose:	q.d.
mode of admin.:	per os, oral tablets
batch no.:	PD-2718 (placebo 100 mg); PD-2674 (placebo 200 mg)
Duration of treatment:	12 to 24 weeks Patients having a clinical response considered meaningful (defined by $PASI_{50}$) at the end of the 12-week treatment period with a satisfactory safety experience were eligible to enter a treatment extension phase of 12 weeks
Criteria for evaluation:	Primary efficacy endpoint: Achievement of ≥75% reduction from baseline in PASI score ($PASI_{75}$) at 12 weeks Secondary efficacy endpoints: Other PASI assessments: Achievement of ≥75% reduction from baseline in PASI score ($PASI_{75}$) at 24 weeks; achievement of ≥50% reduction from baseline in PASI score ($PASI_{50}$) at 12 and 24 weeks; achievement of ≥90% reduction from baseline in PASI score ($PASI_{90}$) at 12 and 24 weeks Time to sustained $PASI_{50}$ and sustained $PASI_{75}$ among $PASI_{75}$ achievers at 12 weeks; time to sustained $PASI_{50}$ among $PASI_{50}$ achievers any time during the study (within 24 weeks); time to sustained $PASI_{50}$ and sustained $PASI_{75}$ among all patients

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Criteria for evaluation: (continued)	Absolute and percent changes from baseline in PASI scores; absolute and percent changes from baseline in PASI subscores (thickness, erythema, scaling) NPF Psoriasis Score "Static Physician Global Assessment (sPGA)": Achievement of sPGA clear or almost clear at Week 12 and 24; achievement of sPGA clear, almost clear or mild at Week 12 and 24; absolute change from baseline in sPGA at 12 and 24 weeks NPF Psoriasis Score Assessments (other than sPGA): Assessment of induration at two target lesions; Patient Global Assessment of Rank severity of psoriasis (PGAR); Body Surface Area (BSA) covered with disease (BSAD); Patient's Assessment of Itch (PAI) Discontinuations of therapy due to lack of efficacy Relapse and rebound: Incidence of relapse and rebound during treatment with study drug and 8 weeks follow-up period Dermatology Life Quality Index (DLQI): Change of DLQI score (quantitative) from baseline at 12 and 24 weeks; achievement of at least 5 points reduction on DLQI score from baseline at 12 and 24 weeks; combined achievement of at least 5 points reduction on DLQI score and PASI75 from baseline at 12 weeks Pain Visual Analog Scale for patients with psoriatic arthritis
Efficacy / clinical pharmacology:	Population pharmacokinetics
Safety:	Incidence of adverse events, changes on physical examination and vital signs, changes in safety laboratory analyses and ECG, discontinuation of therapy due to an adverse event
Statistical methods:	Primary endpoint $PASI_{75}$ analysed with Fisher's exact test. Analysis of covariance, Cochran Mantel-Haenszel test, Wilcoxon rank sum test and log rank test for secondary endpoints. For sPGA validation: correlations/concordance indices for reproducibility analyses, correlations and diagnostic / predictive indices for relationships with other measurements.

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SUMMARY – CONCLUSIONS:

Efficacy / clinical pharmacology results:	The trial was discontinued prematurely because of new preclinical safety findings of cardiac toxicity in mice; therefore, only limited efficacy data were obtained. PASI scores at the End of Treatment showed a slight excess of patients attaining PASI 75 and PASI 50 scores among patients in the BIRT 2584 XX 300 mg treatment group. Mean PASI scores at Weeks 8 and 12 showed trends towards lower scores in the BIRT 2584 XX 300 mg dose group. Static PGA also showed a weak trend towards improvement with increasing BIRT 2584 XX dose. However, in view of the limited number of patients completing 8 and 12 weeks of treatment, the present study cannot be considered an adequate evaluation of the efficacy of BIRT 2584 XX in the treatment of chronic plaque psoriasis.
Safety results:	BIRT 2584 XX appeared to be generally well tolerated in this study. Most observed adverse events (AEs) were mild to moderate in intensity. Diarrhea and pruritis were the only AEs that appeared to show a dose relationship to BIRT 2584 XX treatment. There were two serious adverse events (SAEs), neither of which was considered related to treatment. There were no notable abnormalities of safety laboratory tests, vital signs, physical examination, or ECG that were considered relevant to treatment. The post-treatment assessments, including the 1 year follow-up, did not show any evidence of cardiac toxicity.
Conclusions:	Overall, while weak trends in favour of BIRT 2584 XX treatment were observed among the secondary efficacy parameters, the study cannot be considered an adequate evaluation of the efficacy of BIRT 2584 XX in the treatment of chronic plaque psoriasis. BIRT 2584 XX appeared to be generally well tolerated in this study, and there was no evidence of cardiac toxicity.