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Study No: DPB102761	
Title : An Open-Label, Randomized Study with 3 Cohorts of 3-Way Crossovers to Investigate the Safety, Tolerability and Pharmacokinetics of <i>XX</i> mg Oral Doses of <i>Investigational Drug</i> and 500mg BID Oral Doses of Metformin (Cohort 1), 8mg Oral Doses of Rosiglitazone (Cohort 2), and 45mg Oral Doses of Pioglitazone (Cohort 3)	
Rationale: This study is being performed to assess the potential for pharmacokinetic interactions between <i>Investigational Drug</i> and other oral agents (metformin, rosiglitazone, pioglitazone) that are likely to be co-administered for the treatment of T2DM. Since the <i>Investigational Drug</i> is not a marketed product only information related to the treatment period of rosiglitazone alone will be presented. Further information may be summarized in the future	
Phase: I	
Study Period: January 11, 2006 to June 18, 2006	
Study Design: This study was composed of three open label, randomized, three period crossovers conducted within three separate cohorts. Each cohort will be composed of 3 phases (Screening, Treatment, and Follow-up). The Treatment phase will be divided into 3 periods. Each period will last 7 days and will be separated by a washout period of 21 days. During the treatment Phase, subjects will be randomized into one of three cohorts (metformin, rosiglitazone, or pioglitazone). Subjects in the rosiglitazone Cohort received each of the following three treatments in a randomized, crossover fashion: Treatment A = <i>XX</i> mg <i>Investigational Drug</i> , QD for 7 days; Treatment B = 8mg rosiglitazone, QD for 7 days Treatment C = <i>XX</i> mg <i>Investigational Drug</i> + 8mg rosiglitazone, QD for 7 days	
Centres: One study centre in Canada	
Indication: Type 2 Diabetes Mellitus	
Treatment: 8 mg of rosiglitazone; Treatment Period: rosiglitazone for 7 days	
Objectives: The primary objectives of this study are (1) to determine exposures (AUC(0- τ) and C _{max}) of <i>XX</i> mg daily doses of <i>Investigational Drug</i> when administered alone and when coadministered with metformin, rosiglitazone, and pioglitazone for 7 days, and (2) to determine exposures (AUC(0- τ) and C _{max}) of metformin, rosiglitazone, and pioglitazone (including active pioglitazone metabolites) when administered alone and when coadministered with <i>XX</i> mg daily doses of <i>Investigational Drug</i> for 7 days.	
Statistical Methods: A sufficient number of subjects were to be enrolled to ensure that at least 18 subjects completed each cohort. Pharmacokinetic analysis of the plasma rosiglitazone concentration-time data was conducted using noncompartmental Model. Actual elapsed time from dosing was used to estimate all individual plasma PK parameters. Descriptive summaries included n, mean, standard deviation, median, minimum, and maximum for continuous variables, n and percent for categorical variables, geometric mean, 95% confidence interval (CI), and the between-subject CV (%CV _b) based on geometric mean for the log-transformed PK parameters. Safety parameters including AEs, clinical laboratory evaluations, physical examination findings, vital sign measurements, and 12-lead ECG results were listed and summarized by cohort. All subjects enrolled into the study who received ≥ 1 dose of study drug were included in the safety population. The pharmacokinetic population included all subjects with pharmacokinetic samples adequate for the calculation of pharmacokinetic parameters.	
Study Population: Eligible subjects were healthy male and female (non-child bearing potential) volunteers between 18 and 50 years of age (inclusive).	
Number of Subjects: (<i>Only rosiglitazone data are presented</i>)	All Subjects
Planned, N	Sufficient to achieve 18 completed subjects
Dosed, n (%)	24
Completed, n (%)	24 (100%)
Total Number Subjects Withdrawn, n (%)	0 (0%)
Withdrawn due to Adverse Events, n (%)	0 (0%)
Withdrawn for Other Reasons n (%)	0 (0%)

Demographics	
N (Safety Population)	24
Females: Males	8:16
Mean Age in Years (SD)	39.1 (7.82)
Mean Weight in Kg (SD)	72.04 (14.27)
White, n (%)	16 (67%)
African American, n (%)	4 (17%)
Pharmacokinetics for rosiglitazone:	
Parameter^a	
C _{max} , ng/mL	554 (28)
AUC (0-tau), hr*ng/mL	2668 (32)
T _{1/2} , hr	3.4 (22)
T _{max} , hr	3.4 (2.4, 5.3)
a. For C _{max} , AUC and t _{1/2} the geometric mean (%C _{vb}) is presented. For T _{max} the median and range is presented.	
Safety results: An on therapy AE was defined as one which occurred after administration of study medication and on or before the final follow-up visit.	
Adverse Events:	Rosiglitazone Alone Administration Period
N (Safety Population)	24
No. subjects with AEs, n (%)	8 (33)
Constipation	2 (8)
Abdominal pain	2 (8)
Serious Adverse Events, n (%) [n considered by the investigator to be related, possibly related, or probably related to study medication]: 0	
There were no deaths reported in this study.	

Publications: No publication
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