These Clinical Trial Results are provided for informational purposes only.

The clinical trial synopses are supplied for information purposes only. The information does not replace the official labelling of a given drug product, which presents benefits and risks of the product for approved use(s) based on an evaluation of an entire research program.

Clinical trials may include approved and non-approved uses, formulations or treatment regimens. The information provided is not intended to promote any product or indication and is not intended to replace the advice of a healthcare professional. If you have questions about this information, please consult a healthcare professional. Before prescribing any Daiichi Sankyo product(s), healthcare professionals should consult prescribing information for the product(s) approved in their country.

REPORT SYNOPSIS

Name of Sponsor/Company: Daiichi Sankyo Pharma Development Name of Test Product: Rivoglitazone HCl (CS-011) Name of Active Ingredient: Rivoglitazone HCl	Individual Study Table Referring to Part of the Dossier Volume: Page:	*(For National Authority Use Only)*

Title of Study:	A Randomized, Double-Blind, Placebo and Active Comparator-Controlled, Parallel-Group Study of the Efficacy and Safety of Rivoglitazone as Monotherapy Treatment of Type 2 Diabetes Mellitus (CS0011-A-U302)
Phase of Development:	3
Study Period:	First subject first visit date: 14 Nov 2007 Last subject last follow-up visit date: 23 May 2008 Daiichi Sankyo Pharma Development terminated this study on 23 Apr 2008 because of changes in the clinical development plan with 94, of the 2600 planned, randomized subjects.
Investigator(s):	For a complete list of investigators, see Appendix 16.1.4.
Study Center(s):	73 sites in the United States (US) 22 sites in India
Publication (reference):	N/A
Study Objectives/Hypothesis:	The primary objective of the study was to compare the effects on mean change from baseline in glycosylated hemoglobin (A_{1c}) for rivoglitazone versus pioglitazone administered as monotherapy in type 2 diabetics over a 26-week treatment period. The secondary objectives of the study were the following: • To demonstrate the safety and tolerability of rivoglitazone as a treatment for type 2 diabetes mellitus; • To demonstrate the lowering of fasting plasma glucose (FPG) with rivoglitazone, versus placebo, over 26 weeks in type 2 diabetics;

Name of Sponsor/Company: Daiichi Sankyo Pharma Development	Individual Study Table Referring to Part of the Dossier Volume: Page:	*(For National Authority Use Only)*
Name of Test Product: Rivoglitazone HCl (CS-011)		
Name of Active Ingredient: Rivoglitazone HCl		

	• To assess the effects of each rivoglitazone dose on the percentage of responders as defined by: – Subjects experiencing a decrease of ≥0.7% in A_{1c}; – Subjects achieving an A_{1c} goal of <7.0%; – Subjects achieving an A_{1c} goal of <6.5%; • To assess the effect of rivoglitazone versus placebo on homeostasis model assessment indices of insulin resistance and β-cell function in type 2 diabetics; • To assess the effects of rivoglitazone on change from baseline and percent change from baseline in plasma lipids (including total cholesterol [TC], low-density lipoprotein cholesterol [LDL-C], high-density lipoprotein cholesterol [HDL-C], and triglycerides [TG]), and on other parameters including adiponectin, high-sensitivity C-reactive protein, insulin, apolipoprotein (Apo) A-I, and Apo B; and • To compare the effects of rivoglitazone versus pioglitazone on secondary measures of glycemic control and lipid parameters.
Study Design/Methodology:	This study was planned as a 26-week, multi-center, randomized, double-blind, placebo and active comparator-controlled, parallel-group study in subjects with type 2 diabetes mellitus currently sub-optimally controlled with or without antihyperglycemic (non-thiazolidinedione [TZD]) monotherapy. Subjects not on drug therapy must have been considered by the investigator to have failed diet and exercise as only treatment. Shortly after initiation of the study, the study was terminated by the Sponsor. Consequently, due to the early termination of this study, abbreviated statistical summaries are presented, and only for the primary efficacy variable, secondary efficacy variables, and safety

Name of Sponsor/Company: Daiichi Sankyo Pharma Development	Individual Study Table Referring to Part of the Dossier Volume: Page:	*(For National Authority Use Only)*
Name of Test Product: Rivoglitazone HCl (CS-011)		
Name of Active Ingredient: Rivoglitazone HCl		

	parameters. No formal hypothesis testing was performed due to the limited data available.
Duration of Treatment for Individual Subjects:	The planned total duration of the study was 30 weeks; this included a 2-week, stabilization/washout, placebo run-in period, a 26-week treatment period, and a 2-week post-treatment follow-up period. Due to early termination of the trial, the maximum treatment duration for individual subjects was 18 weeks.
Number of Subjects:	Planned: 2600 Screened: 430 Enrolled/Randomized: 149/94 Completed/Discontinued: 0 completed/94 discontinued
Diagnosis and Main Criteria for Study Entry:	The study population was comprised of subjects diagnosed with type 2 diabetes mellitus who were either untreated (ie, not receiving antihyperglycemic medication within at least 2 months prior to screening) or were treated with a single, non-TZD agent as monotherapy without adequate glycemic control.
Investigational Product and Comparator Information:	1. Dosage Form: rivoglitazone 0.5 mg, 1.0 mg, 1.5 mg Route of Administration: orally, once daily Lot No.: [redacted] Packaging Information: blister cards 2. Dosage Form: rivoglitazone-matching placebo tablet Route of Administration: orally, once daily Lot No.: [redacted] Packaging Information: blister cards 3. Dosage Form: pioglitazone 15 mg, 30 mg, 45 mg Route of Administration: orally, once daily Lot No.: [redacted] Packaging Information: blister cards

Name of Sponsor/Company: Daiichi Sankyo Pharma Development	Individual Study Table Referring to Part of the Dossier Volume: Page:	*(For National Authority Use Only)*
Name of Test Product: Rivoglitazone HCl (CS-011)		
Name of Active Ingredient: Rivoglitazone HCl		

4. Dosage Form: pioglitazone-matching placebo capsule
   Route of Administration: orally, once daily
   Lot No.: [redacted]
   Packaging Information: blister cards

Criteria for Evaluation:

Efficacy: The primary efficacy variable was the change in A_{1c} from baseline to Week 26.

The secondary efficacy variables included the following:

- Change in FPG from baseline to Week 26;
- Changes in A_{1c} from baseline to Weeks 2, 4, 6, 8, 10, 12, 16, 20, and 24;
- Changes in FPG from baseline to Weeks 2, 4, 8, 12, 16, 20, and 24; and
- Percent changes in TC, TG, LDL-C, HDL-C, Apo A-I, and Apo B from baseline to Weeks 12 and 26.

Safety: Safety assessments included adverse events, clinical laboratory parameters (including urinalysis, hematology, and serum chemistry test results), vital signs, physical examinations, prior and concomitant medications, and 12-lead electrocardiogram (ECG) results.

Statistical Methods:

Summary statistics are presented by treatment group. For continuous variables, the number of available observations (n), mean, standard deviation, median, and range are provided. For categorical variables, the frequency and percentage in each category are displayed.

Due to the early termination of the study, statistical summaries are presented for the primary and secondary efficacy variables. No formal hypothesis testing was performed due to the limited data available at the time of study termination.

Summary:

Efficacy Results: Due to the small number of subjects randomized and the early termination of the study, no conclusions on the efficacy of rivoglitazone compared to placebo or pioglitazone could be determined.

Name of Sponsor/Company: Daiichi Sankyo Pharma Development	Individual Study Table Referring to Part of the Dossier Volume: Page:	*(For National Authority Use Only)*
Name of Test Product: Rivoglitazone HCl (CS-011)		
Name of Active Ingredient: Rivoglitazone HCl		

Safety Results: The overall mean duration of exposure to study medication was 50.8 days with the range of mean duration of exposure of 27.0 days to 65.0 days across the 7 treatment groups. Thirty-two (34.4%) subjects had a treatment-emergent adverse event (TEAE): 5 (55.6%) in the rivoglitazone 0.5 mg group, 3 (25.0%) in the rivoglitazone 1.0 mg group, 8 (29.6%) in the rivoglitazone 1.5 mg group, 4 (50.0%) in the pioglitazone 15 mg group, 2 (20%) in the pioglitazone 30 mg group, and 10 (41.7%) in the pioglitazone 45 mg group. Seven (7.5%) subjects had a TEAE that was considered by the investigator to be related to study medication: 1 (11.1%) in the rivoglitazone 0.5 mg group (flank pain and hyperhidrosis), 3 (11.1%) in the rivoglitazone 1.5 mg group (flatulence, peripheral edema, and upper respiratory tract infection), and 3 (12.5%) in the pioglitazone 45 mg group (nausea, edema, peripheral edema, and increased blood creatine phosphokinase). All of the TEAEs were mild or moderate in severity.

No subjects died or had a serious adverse event during the study. No randomized subject discontinued from the study due to a TEAE.

No clinically meaningful safety findings or trends in safety laboratory parameters, weight, vital signs, or ECG parameters were noted.

Due to the small number of subjects randomized and the early termination of the study, comparisons between treatment groups regarding the safety of study medication could not be deduced.

Conclusions: Due to the small number of randomized subjects included in the efficacy summaries, no conclusions can be inferred on the effects of rivoglitazone compared to placebo or pioglitazone on A_{1c}, FPG, lipids, or apolipoproteins. The very limited safety information available did not reveal any unexpected safety or tolerability issues for rivoglitazone or pioglitazone.

Date of the Report: 19 Nov 2008