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Press Announcement
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Press Release

RIMONABANT STUDY SHOWS SIGNIFICANT IMPROVEMENTS IN HbA1c AND CARDIOMETABOLIC RISK FACTORS IN PEOPLE WITH TYPE 2 DIABETES

Results from RIO-Diabetes trial presented at the annual congress of the American Diabetes Association in San Diego

Liège, Belgium, June 12, 2005 – The reported results of a one-year phase III study in 1045 people with type 2 diabetes treated with rimonabant, the first in a new class of therapeutic agents called selective CB_1 Blockers, were that rimonabant 20 mg significantly improved HbA1c (a measure of blood sugar control), dyslipidemia (abnormal levels of fat in the blood), and systolic blood pressure with a concomitant substantial reduction in abdominal obesity in people with type 2 diabetes treated with oral anti-diabetic medications and requiring further control. The study also evaluated the safety and tolerability profile of rimonabant versus placebo in people with type 2 diabetes.

The one-year results of the RIO-Diabetes trial were presented today at the Scientific Sessions of the American Diabetes Association in San Diego, California by André Scheen, Head of the Clinical Pharmacology, Division of Diabetes, Nutrition and Metabolic Disorders, Academic Hospital of Liege, University of Liege, Belgium, principal investigator of the RIO-Diabetes study and a member of the RIO program steering committee.

“The RIO-Diabetes trial results indicated that rimonabant delivered a clinically meaningful reduction in HbA1c and may offer a broad range of cardiometabolic risk factor improvements that are essential for the comprehensive management of people with type 2 diabetes,” said Professor Scheen.

RIO-Diabetes Objectives and Design

The RIO-Diabetes trial is one of four phase III studies comprising the RIO program, which assessed the efficacy and safety of rimonabant in cardiometabolic risk factor improvement and weight loss in over 6,600 overweight and obese patients studied world-wide. All four trials in the phase III program have been completed.

RIO-Diabetes is a phase III, multinational, multicenter, randomized, double-blind, and placebo-controlled trial comparing two fixed-dose regimens of rimonabant (5 mg and 20 mg once daily) to placebo for a period of one year. The study was conducted on 1,045 people with type 2 diabetes at 151 centers in 11 countries. The objectives of the trial were to assess the efficacy and safety of rimonabant in patients with type 2 diabetes already being treated with either metformin or sulfonylurea. The study investigated the effect of rimonabant on HbA1c, waist circumference, body weight and other cardiometabolic risk factors such as dyslipidemia and blood pressure as well as metabolic syndrome. Safety and tolerability were also evaluated over the one-year treatment period.

RIO-Diabetes Findings

Among all patients who entered the RIO-Diabetes study, patients on rimonabant 20mg achieved an HbA1c reduction of 0.7% versus placebo ($p<0.001$) from a baseline value of 7.3%. Forty three percent of patients on rimonabant 20mg versus only 21% of those on placebo ($p<0.001$) achieved an HbA1c level below 6.5%, the target treatment goal set by the International Diabetes Federation (IDF)[1] and the American Association of Clinical Endocrinologists (AACE) [2]. Among patients whose baseline HbA1c was higher than 7%, the American Diabetes Association[3] treatment goal, 52.7% of patients on rimonabant 20mg vs. 26.8% of patients on placebo ($p<0.001$) reduced their HbA1c to below this goal by the end of the study. More than 50% of the improvement in HbA1c observed with rimonabant 20mg was calculated to be beyond that attributable to the weight loss achieved ($p<0.001$).

“What is noteworthy about the findings of the RIO-Diabetes trial is that even in a patient population with an average HbA1c level at a point where further control is difficult to achieve, rimonabant was still able to achieve a clinically significant reduction in HbA1c,” said Professor Scheen.

Weight was reduced by 5.3 kg (11.7 lbs) in patients treated with rimonabant 20 mg/day vs. 1.4 kg (3 lbs) for patients in the placebo group ($p<0.001$). In addition, patients treated with rimonabant 20mg benefited from a reduction in waist circumference of 5.2 cm (2 in) versus 1.9 cm (0.7 in) observed in the placebo group ($p<0.001$).

“The weight loss reported for rimonabant in patients with diabetes may be an important finding,” said Dr. Michael D. Jensen, Professor of Medicine, Mayo Clinic College of Medicine, Rochester, Minnesota. “Glycemic control with current therapies is often associated with weight gain. This weight gain can diminish the benefits of treatment and lessen the overall improvement in cardiometabolic risk,” he added.

HDL-cholesterol and triglycerides were significantly improved in patients treated with rimonabant 20 mg/day throughout the one year period. Among all patients who entered the study, HDL-cholesterol increased by 15.4% in the rimonabant 20 mg/day group vs 7.1% in the placebo group (rimonabant 20 mg/day vs placebo ($p<0.001$), a difference compared to placebo of 8.3%).

Furthermore, triglycerides were reduced by 9.1% in patients treated with rimonabant 20 mg/day compared to an increase of 7.3% in the placebo group (p<0.001), a difference compared to placebo of 16.4%. As was the case with HbA1c, more than 50% of the improvement in HDL levels were calculated to be beyond that attributable to the weight loss achieved (p<0.001). In addition to the improvements in lipid profiles, a reduction of 18.9% in the prevalence of patients meeting the criteria for metabolic syndrome was observed in the 20mg group compared to 7.6% in the placebo group (p=0.007). Metabolic syndrome is a constellation of metabolic abnormalities linked to abdominal obesity such as elevated fasting glucose, high waist circumference, atherogenic dyslipidemia (low HDL cholesterol or high triglycerides) and elevated blood pressure, all of which are associated with an increased risk of cardiovascular disease.[4]

RIO – Diabetes safety & tolerability

The RIO Diabetes study also assessed the safety and tolerability of rimonabant 20 mg, 5mg and placebo, the results of which were consistent with the data from the entire rimonabant phase III trial program involving 6,600 patients. Side effects were mainly mild and transient and most frequently included nausea (12.1% for rimonabant 20 mg/day vs.5.7% for placebo), dizziness (9.1% for rimonabant 20 mg/day vs. 4.9% for placebo), diarrhea (7.4% for rimonabant 20 mg/day vs. 6.6% for placebo), vomiting (5.9% for rimonabant 20 mg/day vs. 2.3% for placebo), hypoglycemia (5.3% for rimonabant 20mg/day vs. 1.7% for placebo), fatigue (5.3% for rimonabant 20mg/day vs 3.7% for placebo) and anxiety (5.0% for rimonabant 20mg/day vs 2.6% for placebo) . Discontinuation rates due to adverse events were consistent with those reported in other trials in the RIO program (13.8% versus 7.2% in the rimonabant 20mg and placebo arms respectively at one year across all four RIO trials).

Intra-abdominal adiposity and Diabetes

A global pandemic of diabetes is underway, with the number of diabetic individuals projected to rise from 194 million today to 333 million by 2025.[5] Type 2 diabetes is associated with a sharply increased risk of cardiovascular disease and the higher prevalence of abdominal obesity and other cardiometabolic risk factors associated with the metabolic syndrome in people with type 2 diabetes accounts for the majority of this risk. Recent findings have shown that abdominal obesity is a much better predictor of heart attack than weight or BMI.[6] Abdominal obesity can be measured simply by waist circumference [7], and is an indicator of intra-abdominal adiposity, the hidden fat present deep within the abdomen [8]. Men with a waist circumference of more than 102 cm (40 in.) and women whose waist circumference exceeds 88 cm (35 in) are considered to be abdominally obese, as defined by NCEP ATPIII guidelines. [9]

Rimonabant

Rimonabant is the first in a new class of drugs called CB_1 blockers. By selectively blocking CB_1 receptors both centrally and peripherally in fat cells and liver cells, rimonabant helps to normalize an overactive EC System.

The RIO-Diabetes trial was sponsored by Sanofi-Aventis.

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