These results are supplied for informational purposes only.
Prescribing decisions should be made based on the approved package insert in the country of prescription.

Sponsor/Company:	sanofi-aventis	**Study identifier:**	NCT00481975
Drug substance:	rimonabant	**Study Code:**	ACT3801
		Date:	24 May 2007

Title of the study:	A randomized, double-blind, placebo-controlled, parallel-group, fixed-dose, multicenter study to assess efficacy and safety of rimonabant 20 mg versus placebo on weight loss and frequency of binge episodes in obese patients with food craving.
Principal investigator:	Prof. Aila Rissanen, Obesity Research Unit, Finland
Study centers:	29 active sites in 7 countries (France, Finland, Netherlands, Portugal, Sweden, Switzerland, and the United States)
Publications:	Not applicable
Study period: Date first patient enrolled: 13 August 2004 Date last patient completed: 10 August 2005	**Phase of development:** Phase 3
Objectives: Primary: Secondary:	To assess the effect of rimonabant compared to placebo on weight loss over a period of 6 months when prescribed with a hypocaloric diet in obese patients with binge eating disorder (BED). • to assess the effect of rimonabant on the number of binge episodes per week in the study population; • to assess the effect of rimonabant on eating behavior using the Binge Eating Scale (BES) and Three Factor Eating Questionnaire (TFEQ) in the study population; • to evaluate the safety and tolerability of rimonabant over a period of 6 months.
Methodology:	This was a multicenter, randomized, double-blind, placebo-controlled, parallel-group, fixed-dose regimen (20 mg rimonabant once daily), 6 month, phase 3 study. Following a 15-day screening period, patients were randomly allocated to placebo or 20 mg of rimonabant using a randomization ratio of 1:1. Patients received the investigational product for 6-months in a double-blind manner in conjunction with a mild hypocaloric diet.
Number of patients:	Planned: 200 Randomized: 289 Treated: 289

Diagnosis and criteria for inclusion:	a) Male or female patients aged ≥18 and ≤70 years b) Body Mass Index (BMI) ≥30 to ≤45 kg/m² c) Diagnosis of eating disorder using The Questionnaire on Eating and Weight Patterns (QEWP-R) for diagnosing Eating Behaviors: • Recurrent episodes of binge eating. An episode of binge eating was characterized by both of the following: - eating, in a discrete period of time (eg, within any 2-hour period), an amount of food that is definitely larger than most people would eat in a similar period of time under similar circumstances; and - a sense of lack of control over eating during the episode (eg, a feeling that one cannot stop eating or control what or how much one is eating); • The binge-eating episodes were associated with 3 (or more) of the following: - eating much more rapidly than normal; - eating until feeling uncomfortably full; - eating large amounts of food when not feeling physically hungry; - eating alone because of being embarrassed by how much one is eating; - feeling disgusted with oneself, depressed, or very guilty after overeating. • Marked distress regarding binge eating was present; • The binge eating occurred, on average, at least 1 day a week for 6 months; • The binge eating was not associated with the regular use of inappropriate compensatory behaviors (eg, purging, fasting, excessive exercise) and did not occur exclusively during the course of Anorexia Nervosa or Bulimia Nervosa.	
Investigational product: Dose: Administration:	rimonabant 20 mg once daily oral administration in the morning before breakfast	
Duration of treatment:	6 months	**Duration of observation:** Approximately 28 weeks [including a 15 day screening period and a 6 month (26 week) treatment period]
Reference therapy: Dose: Administration:	placebo (identical in appearance to the rimonabant capsules) once daily not applicable oral administration in the morning before breakfast	
Criteria for evaluation:		
Efficacy:	The primary efficacy assessment was the change in body weight from baseline to Day 180 visit (Visit 9, Month 6). Secondary efficacy assessments included: • binge eating episodes; • BES; • eating behavior using the TFEQ; • waist circumference; • BMI.	
Safety:	Safety was assessed by spontaneously reported adverse events (AEs), vital signs assessments (blood pressure [BP] and heart rate [HR]), physical examinations, and Hospital Anxiety and Depression (HAD) scale.	

Statistical methods:	Efficacy analysis was performed on the intent-to-treat (ITT) population, ie, all patients randomized and exposed having at least 1 post-baseline evaluation for a given parameter. In addition, the completer population, which consisted of a subset of patients from the ITT population classified with a completed study treatment period, from the case report form (CRF) end form, was also used for the analysis of weight and response rates on binge episodes, in case its size was less than 90% of the intent-to-treat population size. Efficacy was also assessed in the DMS-IV Binge Eating Disorder population (defined as patients with at least 2 binge days per week). For the safety analyses, the population consisted of all randomized patients who had at least 1 dose of double-blind study drug and was used as the reference population in the overall clinical (adverse events) safety analyses. For quantitative/continuous efficacy variables, for parameters not associated with any baseline measurement, a one-way analysis of variance with treatment as fixed effect was used. Otherwise analysis of covariance using the baseline value as covariate and with treatment as fixed effect was used. The model included the interaction term of the covariate and treatment. This interaction term was to be removed from the model if non-significant at the 5% level. The adjusted least squares (LS) means were computed and the comparisons were performed using a Student's test. The last observation carried forward (LOCF) approach was used in case of missing data.
Summary:	A total of 289 patients were randomized, 205 (70.9%) completed treatment. The demographic characteristics of all exposed patients were similar across treatment groups and were mostly women and Caucasian, and a large percentage of subjects had morbid obesity (24.2%).
Efficacy results:	At six months, a significantly greater body weight loss from baseline was seen in patients treated with rimonabant when compared to placebo ($p<0.0001$). In the ITT population, at 6 months, the LS mean (±SE) decrease in body weight from baseline was 4.8 (±0.4) kg in patients treated with rimonabant compared to 0.4 (0.4) kg in patients treated with placebo. Similar results were observed in the analysis by class of responders in patients with 5% ($p<0.0001$) and 10% ($p=0.0016$) body weight loss, respectively. In the ITT population, a greater number of patients treated with rimonabant (78.7%) met the response definition (>=50% reduction in binge per week frequency) when compared with placebo (69.1%) ($p=0.0657$). However, in the population with BED according to DSM-IV, a significantly ($p=0.04$) greater number of patients treated with rimonabant (80.0%) met the same response definition when compared with placebo (68.4%). In the ITT population using another responder definition (decrease >=2 binge episodes per week), a statistically significantly ($p=0.0086$) greater number of patients treated with rimonabant (68.1%; 96/141) met the new responder definition when compared with placebo (52.8%; 75/142). In the ITT population, with respect to reduction in number of binge episodes per week, no differences ($p=0.5299$) between rimonabant and placebo were observed. Similarly, in the DSM-IV population, no difference in ($p=0.5215$) the number of binge episodes per week between rimonabant and placebo was observed. The evaluation of binge eating utilizing the BES at six months, showed that patients treated with rimonabant had a significantly ($p=0.0208$) greater reduction in binge eating from baseline when compared with patients treated with placebo. Similarly in the DSM-IV population, at 6 months, patients treated with rimonabant showed a significantly ($p=0.0077$) greater reduction in binge eating from baseline when compared with patients treated with placebo.

Summary (continued):

Efficacy results (continued):

The evaluation of eating behavior utilizing the TFEQ (both in the ITT and DSM-IV populations) showed that patients treated with rimonabant showed a greater increase in their dietary restraint, a greater reduction in disinhibition, and a greater reduction in hunger when compared with patients treated with placebo; however none of these differences were statistically significant.

Safety results:

Treatment-emergent adverse event(s) (TEAEs) were reported more frequently in the rimonabant group compared with the placebo group. The numbers (%) of randomized and exposed patients experiencing at least 1 TEAE are presented in the table below:

	Placebo (N=146) N (%)	**Rimonabant (N=143) N (%)**
Subjects with any TEAE	111 (76.0)	118 (82.5)
Subjects with any SAE	2 (1.4)	2 (1.4)
Deaths	0 (0)	0 (0)
Subjects permanently discontinued due to TEAE	9 (6.2)	19 (13.3)

In the rimonabant group, individual TEAEs reported in ≥5% of rimonabant patients and more frequently (≥1% difference) than in the placebo group are presented in the table below and included nausea, nasopharyngitis, diarrhoea, insomnia, anxiety, depression, and vomiting.

Preferred Term	**Placebo (N=146) N (%)**	**Rimonabant (N=143) N (%)**
Nausea	6 (4.1)	43 (30.1)
Nasopharyngitis	24 (16.4)	29 (20.3)
Diarrhoea	10 (6.8)	13 (9.1)
Insomnia	4 (2.7)	11 (7.7)
Anxiety	4 (2.7)	9 (6.3)
Depression	6 (4.1)	9 (6.3)
Vomiting	2 (1.4)	8 (5.6)

Two patients each in the rimonabant and placebo groups experienced serious adverse events, with none with reasonable drug relationship. There were no deaths during the study period. Nineteen (13.3%) patients in the rimonabant group had TEAEs leading to discontinuation. The most frequently reported TEAEs leading to discontinuation were nausea (5 patients), depression (3 patients), and insomnia (3 patients).

Date of full report: 24 August 2006