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Sponsor / Company: sanofi-aventis **Drug substance(s):** SAR407899	**Study Identifier:** NCT00914277 **Study code:** ACT10775
Title of the study: Randomized, double-blind, placebo and active controlled study of the activity of SAR407899 single-dose on the ability to increase duration of penile rigidity, under experimental condition, in patients with mild to moderate erectile dysfunction	
Study center(s): SGS Aster, Phase I Research Unit, 3 and 5 Rue Eugène Millon, 75015, Paris, FRANCE	
Study period: Date first patient enrolled: 26/May/2009 Date last patient completed: 26/Oct/2009	
Phase of development: 2	
Objectives: This study was planned to: Determine and compare the effect of SAR407899 versus placebo after single dose administration, in patients suffering from mild to moderate erectile dysfunction, on the duration of penile rigidity: - Duration of penile rigidity ≥ 60% at the tip of the penis, - Duration of penile rigidity ≥ 80% at the base and the tip of the penis. Assess the safety including specific monitoring of effects on blood pressure.	
Methodology: Single center, randomized double-blind, double dummy, 4 arm crossover study	
Number of patients: Planned: 24 Randomized: 24 Treated: 24 Evaluated: - Pharmacodynamic: 24, - Safety: 24, - Pharmacokinetics: Not applicable	
Diagnosis and criteria for inclusion: Male patients aged between 18 to 60 years with mild to moderate Erectile Dysfunction (ED)	

Investigational product: SAR407899 1 mg and 10 mg capsules and matching placebo

Dose: 15 and 20mg single dose

Administration: Oral

Duration of treatment: 4 days

Duration of observation: 28 days

Reference therapy: Sildenafil and matching placebo

Dose: 50 mg

Administration: Oral

Criteria for evaluation:

Efficacy

All efficacy outcome endpoints were based on RigiScan® Plus recordings that started 30 minutes prior to dosing and ended approximately 4 hours after study drug dosing. During this recording period, beginning 2 hours after single dose SAR407899 / SAR407899 placebo dosing and 1 hour after single dose Sildenafil / Sildenafil placebo administration, visual sexual stimulation was provided to the patient in the form of sexually explicit videos viewed for three 20 minute periods separated by a 20 minute non-viewing rest period.

Safety

Overall clinical safety was ensured and monitored by physical and clinical examinations, adverse event recording, measurement of vital signs and review of clinical laboratory data and ECG.

Statistical methods:

Efficacy

The primary endpoint (duration of penile rigidity ≥60% at the base of the penis assessed by RigiScan® Plus) was analyzed using a linear mixed effects model with fixed terms for sequence, period, treatment, and random terms for patient within sequence. Estimates with 95% confidence intervals for the difference of the mean treatment effect were obtained from the model. The effect of Sildenafil compared to placebo was assessed to establish the sensitivity of the study. The effect of SAR407899 was assessed by comparing each dose to placebo. No adjustment for multiplicity was applied due to the exploratory nature of this proof of concept study.

Data from the secondary endpoints were analyzed using the same approach.

Safety

General evaluation of safety and tolerability was based on the review of individual values and summary statistics. Treatment Emergent Adverse Events (TEAE) were tabulated by counts and percentages. Changes in ECG and vital signs were examined against pre-defined criteria for Potentially Clinically Significant Abnormalities (PCSA) and were tabulated by counts.

Summary:

Demography and baseline characteristics

A total of 24 patients were randomized and all completed the study. The mean age of patients was 49 ± 8 years, ranging from 25 to 59 years. The mean duration of ED was 5 ± 5 years (range 1-24 years).

Efficacy results

Duration of rigidity ≥ 60% at the base of the penis was 30 minutes, 42 minutes, 53 minutes and 60 minutes in placebo, SAR407899 15mg, SAR407899 20mg and Sildenafil groups respectively. The differences versus placebo were statistically significant in all groups.

The mean number of observed erections was around 3 in all groups, with a mean duration of an erection of 15 minutes for placebo, 17 minutes for SAR407899 15 mg (NS), 23 minutes for SAR407899 20mg (p versus placebo = 0.013) and 27 minutes for Sildenafil (p versus placebo = 0.0002).

Safety results

A total of 24 patients were randomized. All randomized patients received one dose of SAR407899 15 mg, SAR407899 20 mg, Sildenafil 50 mg or placebo at each treatment period. None of the patients experienced any serious TEAE, TEAE leading to death or discontinuation. Few patients experienced TEAE. The main reported TEAE was headache. All patients recovered within less than 1 day.

Six patients had orthostatic SBP hypotension (≤ -20 mmHg). Orthostatic hypotension occurred at different time of the day, mainly between 02H20 and 03H40 post dose. None of the PCSA were associated with TEAE.

Issue date: 21-JAN-2011