Summary ID# 9113

Clinical Study Summary: Study H6D-HL-LVGD

Effect of Tadalafil on the Quality of Life and Sexual Life Satisfaction in Erectile Dysfunction (ED) Patients Previously Treated with Other Oral ED Therapy

Date summary approved by Lilly: 11 March 2008

Title of Study: Effect of Tadalafil on the Quality of Life and Sexual Life Satisfaction in Erectile Dysfunction (ED) Patients Previously Treated with Other Oral ED Therapy

Investigator(s): This multicenter study included one principal investigator and 15 investigators.

Study Center(s): This study was conducted at 15 study centers in 1 country.

Length of Study:
Date of first patient enrolled: 08 October 2004
Date of last patient completed: 27 September 2005

Phase of Development: 4

Objectives:

Primary Objectives:

To test if on-demand therapy with tadalafil, as measured by the Spontaneity domain of the Psychological and Interpersonal Relationship Scales (PAIRS) questionnaire, increases the possibility of spontaneous sexual activity in ED patients compared with any other previous oral ED treatment.

Secondary Objectives:

- Estimate the level of quality of life, measured using the 15D and LiSat-11 scales, in treated ED patients in order to be able to compare it with existing data on the quality of life of the general population and patients suffering from other diseases and symptoms.
- Estimate whether the response to on-demand therapy with tadalafil, compared with previous oral ED treatment, has additional beneficial effects on the psychological/interpersonal aspects of sexual function and general quality of life measured by:
  - The Sexual Self-Confidence and Time Concerns domains' scores of the PAIRS scale;
  - The 15D scale, a validated 15-dimensional health-related quality of life instrument, which has a sexual activity dimension;
  - The LiSat-11 scale, a graded self-perceived life-satisfaction scale;
  - The Global Assessment of Treatment Response (GATR) questions.

Study Design: Multicenter, non-randomized, open-label, 1-arm study comparing the effects of pre-study ED treatment with oral tadalafil 10 or 20 mg taken on demand on psychological and relationship outcomes, patient preference, and quality of life associated with ED in a general practice setting.

Number of Patients: Planned: 200 Randomized: 202 Completed: 197
Diagnosis and Main Criteria for Inclusion: Men aged >18 years, with at least a 3-month history of ED who have been using any oral prescription medication, except tadalafil, for ED, for a minimum period of 3 months immediately before onset of this study, and have responded to the previous medication.
Test Product, Dose, and Mode of Administration: Tadalafil 10 or 20 mg taken orally as needed, not more than once daily. Dosage could be changed between doses twice during the study, if needed.
Reference Therapy, Dose, and Mode of Administration: None
Duration of Treatment: 3 months
Variables: Efficacy: The primary efficacy variable was the change from baseline to endpoint in the Spontaneity domain of the PAIRS scale. Secondary efficacy variables included the change from baseline to endpoint in Sexual Self-Confidence and Time Concerns domains of the PAIRS scale, the Life Satisfaction domain in the LiSat-11 score, the 15D score, the 15D profile, and the changes in GATR responses collected at baseline and endpoint. Safety: Adverse events.
Evaluation Methods: Efficacy analyses included data from all subjects who received at least 1 dose of study medication and who had both a baseline and endpoint score for the relevant questionnaire. The baseline values of the domains of the PAIRS, the 15D scores, and the continuous GATR responses were compared to endpoint values using analysis of variance (ANOVA). The change in the frequency of positive responses to each GATR question between baseline and endpoint were summarized descriptively and analyzed using McNemar's test. The LiSat-11 scale was summarized with descriptive statistics for absolute values and change from baseline to endpoint. The baseline values of the domains were compared to endpoint values using the Wilcoxon signed-rank test. Safety was assessed by evaluating all reported adverse events and vital signs. Safety analyses included data from all subjects who received at least 1 dose of study medication.

Summary:

Of the 202 patients enrolled, 197 (97.5%) completed the study. Four subjects were lost to follow up and 1 subject decided not to continue with the study. The efficacy dataset included 194 patients; patients who did not receive any study medication, who did not provide any postbaseline data, or who did not use erectile dysfunction (ED) treatment prior to enrolling in the study were excluded. The safety dataset included any patient who received study medication (N=201). Tadalafil 10 mg was dispensed to 7% of patients and tadalafil 20 mg was dispensed to 93% of patients.

All patients were Caucasian men. Mean age (standard deviation [SD]) of patients was 57.4 years (9.5). The duration of ED was 1 year or greater for 90.6% of the patients and 71.3% had moderate ED. The etiology of ED was described as being psychogenic for 19.3% of patients, organic for 27.7% of patients, and mixed for 53% of patients. Prior

ED treatment included sildenafil (90%), vardenafil (19%), and apomorphine (5%). In addition to oral medication, 4% of patients had used intracavernous or intraurethral alprostadil, and 6% had received sexual therapy. Preexisting conditions included hypertension (35%), lipid disorders (22%), diabetes (13%), angina pectoris/coronary artery disease (7%), and depression (4%).

Results for Primary and Secondary Objectives

One hundred ninety-four patients provided some data for analysis at baseline and endpoint. Psychological and Interpersonal Relationship Scales (PAIRS) questionnaire data were available at baseline and endpoint for 184 patients. Increases in score for the Spontaneity (primary objective) and Sexual Self-Confidence domains indicate improvement; decreases in score for the Time Concerns domain indicate improvement. There was a statistically significant improvement in all PAIRS domain scores from baseline to study end. From baseline to endpoint the mean (SD) score increased from 3.06 (0.44) to 3.12 (0.40; p =.045) for the Spontaneity domain and from 2.22 (0.61) to 2.74 (0.60; p<.001) for the domain of Sexual Self-Confidence. The mean (SD) score for the Time Concerns domain decreased from 2.56 (0.42) to 2.24 (0.42; p<.001).

Increases in score for the 15D scale indicate improvement. Statistically significant improvement from baseline to endpoint was reported on the 15D dimensions of mobility, depression, distress, and sexual activity. The mean (SD) score increased from 0.94 (0.12) to 0.96 (0.10; p=.01) for mobility, from 0.91 (0.12) to 0.94 (0.11; p=.004) for depression, from 0.89 (0.14) to 0.92 (0.12; p=.001) for distress, and from 0.83 (0.21) to 0.88 (0.18; p=.0004) for sexual activity. Changes from baseline to endpoint in the other 15D dimensions (vision, hearing, breathing, sleeping, eating, speech, elimination, usual activities, mental function, discomfort and symptoms, vitality) were not statistically significant (p>.05).

Increases in score for the LiSat-11 domains indicate improvement. LiSat-11 domain scores increased from a mean (SD) score of 4.70 (0.85) at baseline to 4.84 (0.72) at endpoint for life in general (p=.02), from 4.81 (0.83) to 5.01 (0.75) for leisure (p=.002), from 3.61 (1.15) to 4.61 (1.04) for sexual life (p<0.0001), from 4.54 (1.48) to 4.83 (1.36) for family life (p=.0001), and from 4.68 (1.26) to 5.00 (1.05) for partnership relation (p<.0001). Changes from baseline to endpoint in LiSat-11 vocational situation, economy, contacts, ability to manage self-care, physical health, and psychological health domains were not statistically significant (p>.05).

Global Assessment of Treatment Response (GATR) Question 1 responses indicated that the use of ED tablets increased from a mean of 4.7 tablets during the 4-week baseline interval to 9.7 tablets during the 4-week interval at endpoint (p<.0001). The frequency of intercourse attempts (GATR Question 2) increased from 6.4 at baseline to 10.6 at endpoint (p<.0001). Global Assessment of Treatment Response Question 3 responses indicated that the mean number of successful intercourses increased from 5.0 at baseline to 9.8 at endpoint (p<.001), and that the proportion of successful intercourses increased

from 79% at baseline when using other ED medication to 92% at endpoint after taking tadalafil. The proportion of patients with positive responses to GATR Question 4 ("Has the treatment you have been taking during the last 4 weeks improved your erections?") was 94.8% at both baseline and endpoint (p=1.0). The proportion of patients with positive responses to GATR Question 5 ("If yes [to GATR Question 4], has the treatment improved your ability to engage in sexual activity?") was 97.8% at baseline and 99.5% at endpoint (p=.76).

At the conclusion of the study, 84% of the 187 patients who answered GATR Question 6 ("Which, if any, treatment do you plan to use after the study?") indicated a preference for tadalafil, 10% for sildenafil, 3% for vardenafil, 1% for testosterone injections, and 3% had not decided. The most frequently cited reasons for choosing tadalafil were duration of action (49%), better erections (21%), and confidence the medication works every time (13%).

Safety

At least 1 adverse event was reported by 17% of patients. The adverse events reported by at least 1% of patients were headache (3%), dyspepsia (1.5%), rhinitis (1.5%), myalgia (1.5%), fatigue (1%), dizziness (1%), and flushing (1%). There were no discontinuations due to adverse events.

No deaths were reported during the study.

Serious adverse events were reported in 4 patients: 1) cataract operation; 2) newly diagnosed coronary artery disease, treated twice with percutaneous transluminal coronary angiography (PTCA); 3) myocardial infarction treated by PTCA, followed by post-PTCA thromboembolism to cerebral arteries causing cerebral infarction and aphasia; and 4) thromboembolism of popliteal artery, treated with embolectomy.