Clinical trial protocol

Title
Evaluation of the therapeutic effects of escitalopram in pulmonary hypertension, either primary or associated

Inclusion Criteria:
Subjects who meet all the criteria listed below will be considered for study inclusion:

- Ages Eligible for Study: 18 Years and above, Genders Eligible for Study: Both
- Male or female older than 18 years of age
- Meeting WHO criteria for pulmonary hypertension (mean PAP > 25 mm Hg at rest and pulmonary capillary wedge pressure < 15 mm Hg during right heart catheterization)
- Primary pulmonary hypertension (sporadic or familial)
- or pulmonary hypertension associated with connective tissue diseases
- or pulmonary hypertension associated with HIV infection
- or pulmonary hypertension associated with use of appetite suppressants or other toxic compounds,
- or pulmonary hypertension associated with shunting through a congenital heart defect surgically treated
- Class II or III in the NYHA classification scheme
- With a 6-minute walking test distance between 40 % and 80 % of theoretical values (approximately 50 and 480 m)
- On conventional treatment, with no change in this treatment during the last month preceding the study.
- Conventional treatment includes calcium antagonists or beraprost.
- Subject who consents to participate in the study.

Exclusion Criteria:
Subjects with any of the following clinical features will not be included in the study:

- Pulmonary hypertension related to aortic or mitral valve disease, extrinsic pulmonary vein compression
- Pulmonary hypertension related to hypoxia from respiratory disease with a total lung capacity <70% or TIFFENSEAU index <60% upon testing within the last 6 months
- Chronic obstructive lung disease, interstitial disease, sleep apnea syndrome, alveolar hypoventilation, chronic exposure to high altitudes, neonatal lung disease, alveolar capillary dysplasia
- Pulmonary hypertension associated with portal hypertension
- Pulmonary hypertension secondary to chronic thrombosis and/or embolism (occlusion of the proximal or distal pulmonary arteries by thrombosis)
- In the 6-minute walking test, inability to walk for 6 minutes, for any reason, or walking distance of less than 50 m
- Pregnancy, lactation, women of childbearing potential (if needed, effective contraception will be prescribed)
- History of hypersensitivity to citalopram or to medications structurally related to citalopram
- Treatment with another investigational drug within the 3 months preceding study inclusion
- Cardiovascular, hepatic, neurological or endocrine disease that is clinically significant, or any other significant disease that may interfere with the study protocol or with the interpretation of study findings
- History of drug or alcohol abuse
- Liver failure (except abnormalities related to the right ventricular failure)
- Kidney failure
- Mental status preventing the patient from understanding the nature, objectives, and possible consequences of the study
- Non stabilized psychiatric disorders
- Subject unable to comply with protocol-related constraints (e.g., uncooperative, unable to attend follow-up visits, and probably unable to complete the study).

Start of the study
June 2005
Scheduled duration
3 years

Expected number of patients
30

Trial phase
Phase III

Drug
escitalopram

National multicenter study

Purpose
Phase III, multicenter, randomized, double-blind, placebo-controlled study to evaluate the efficacy of Escitalopram (30 mg/day) in two parallel groups (randomization ratio, escitalopram 2/placebo 1).

Primary Outcomes: To evaluate the efficacy of oral escitalopram at the dosage of 30 mg/day for 16 weeks on the 6-minute walking test in patients with pulmonary hypertension.

Secondary Outcomes: To evaluate after 16 weeks: the efficacy of Escitalopram in improving hemodynamic parameters (right heart catheterization); the efficacy of Escitalopram in improving the NYHA class; the efficacy of Escitalopram in improving the quality of life; the efficacy of Escitalopram in reducing exacerbations of signs or symptoms of the disease that would otherwise require hospital admission or treatment intensification, particularly treatment with Bosentan or intravenous administration of epoprostenol; and the safety of Escitalopram, alone or on top of associated drugs.

Primary objective: to evaluate the efficacy of oral escitalopram at the dosage of 30 mg/day for 16 weeks on the 6-minute walking test in patients with pulmonary hypertension.