

Study Protocol Summary

Study Substance	Levosimendan (Simdax 2,5 mg/ml)
Study Title	Efficacy and safety of pulsed infusions of levosimendan in outpatients with advanced heart failure

DESIGN OF THE CLINICAL TRIAL	
Study Objectives	To compare the effects of a pulsed application of Levosimendan versus placebo on the composite end-point functional capacity and quality of life.
Study Design	Multicenter, double-blind, placebo controlled prospective trial with two study arms
Study Hypothesis	45% of the patients in the Levosimendan group and 20% of the patients in the placebo group will reach the primary endpoint
Sample Size	120 Patients with chronic stable heart failure
Study Centers	8 Austrian, 3 Greek and 3 German Cardiology Medical Centers
Study Population	Patients with chronic stable heart failure NYHA III and IV diagnosed at least 3 month before inclusion, above 20 years of age and both genders
Primary Endpoints	<ul style="list-style-type: none"> ➤ The proportion of patients showing an improvement in the six-minutes walk test of 20% or more and a 15% or higher scoring in the Kansas City Cardiomyopathy Questionnaire (KCCQ) at the end of the 24 week study period.
Secondary Endpoints	<ul style="list-style-type: none"> ➤ Determine the effects of a pulsed application of levosimendan on: <ul style="list-style-type: none"> a) short term (8 weeks from randomization) and long-term (24 weeks from randomization event free survival (cardiac death or heart failure-related hospitalization) b) Components of primary endpoints (6-minute walk test and KCCQ) will be analysed as separate endpoints <p>Cardiac death will be divided into arrhythmic death and pump failure death. Adjudication of endpoints is assigned to the independent Data Safety and Monitoring Board</p>
Tertiary Endpoints	<ul style="list-style-type: none"> ➤ Determine the effects of a pulsed application of levosimendan on: <ul style="list-style-type: none"> a) neurohormonal, inflammatory and myocardial biomarkers (Troponin T, NT-proBNP, C-reactive protein, IL-6, TNF-alpha) b) weight c) dose of diuretics d) creatinine clearance e) cost effectiveness (hospitalizations)