

Abstract (Non Technical)

The goal of the proposed clinical trial is to test the hypothesis that intracoronary delivery of an adenovirus encoding AC_{VI} will improve heart function and reduce symptoms in patients with Class III/IV congestive heart failure.

We propose to conduct a Phase 1 / Phase 2 clinical trial. The clinical trial design will be a randomized, double-blinded, placebo-controlled, single-dose study to evaluate the safety, tolerability and clinical effectiveness of ascending doses of human adenovirus-5 (E1/E3-deleted, replication incompetent) encoding human adenylyl cyclase type VI (AC_{VI}) in patients with congestive heart failure. The vector will be delivered by intracoronary injection. We will also evaluate the effects of Ad5.AC_{VI} on exercise tolerance, symptom severity and hemodynamics measured by right heart catheterization.

Two elements justify the use of human subjects in these experiments. First, the adenovirus vector and method of delivery proposed have been used already in a Phase 1 / Phase 2 placebo-controlled randomized and double-blinded clinical trial in patients with *angina*, and was found to be safe and effective, albeit with an adenovirus containing a different transgene in the treatment of a different cardiovascular disease than that proposed here. Second, patients with severe heart failure have a poor long-term outcome on optimal medical therapies, with 50% of patients dying within 3 years of the onset of severe symptoms.¹