



Efficacy and Safety of the Extracorporeal Liver Assist Device (ELAD[®]) in Subjects with Acute on Chronic Hepatitis (AOCH)

Introduction

Vital Therapies Inc. (VTI), based in San Diego, CA has initiated a pivotal Phase 2B/3 clinical trial in subjects with acute on chronic hepatitis (AOCH). The purpose of this trial is to evaluate the ability of ELAD[®] treatment to stabilize the acute phase of AOCH liver disease as measure by the Model of Endstage Liver Disease (MELD) Score. This trial is also referred to as the SILVER (Stabilization In LiVER disease) study.

What is ELAD[®]?

ELAD[®] stands for Extracorporeal Liver Assist Device. ELAD[®] is a device that is comprised of a dialysis-type pump system and several “metabolically active” cartridges, each containing thousands of hollow fiber capillaries through which the subject’s plasma “ultrafiltrate” fluid is circulated. Within each cartridge chamber, cloned immortalized human liver cells (C3A cells) are grown in the extracapillary space (ECS) of the hollow fibers. These cells have been shown to exhibit certain characteristics of normal liver cells (e.g. albumin synthesis, conversion of ammonia to urea, synthesis of coagulation factors such as factor V etc.) and to be free of infectious or adventitious agents. During clinical therapy, the subject’s ultrafiltrate (plasma-like) is pumped through the lumens (intracapillary space {ICS}) of the hollow fiber cartridge, and presumably, toxins found in the ultrafiltrate diffuse across the membrane where they can be metabolized by the C3A cells. These metabolites, along with albumin and other beneficial proteins produced by the cells, can then diffuse back across the membrane into the ICS and be returned to the subject; thus, possibly preventing further deterioration in the subject’s liver disease enabling liver recovery or a bridge to transplantation.

Study Design

This is a multicenter, open-label, randomized, concurrent control study of subjects with AOCH that will occur across 20 study centers in the United States and up to 10 sites in Europe. Approximately 80 subjects meeting the eligibility requirements of the study will be randomly assigned in a 1:1 ratio to receive either standard medical therapy for AOCH plus treatment with the ELAD[®] system (ELAD[®] group), or standard medical therapy alone (Control group). Subjects with a clinical diagnosis of Acute Alcoholic Hepatitis (AAH) will be stratified between the ELAD[®] group and the Control group. Subjects randomized to the Control group will receive standard medical therapy throughout the study. Subjects randomized to the ELAD[®] group will receive continuous treatment with ELAD[®] for a minimum of 3 days and a maximum of 6 days.

Study Objective and Primary Endpoints

The primary objective of this study is to evaluate the efficacy and safety of ELAD[®] to stabilize liver function during the acute phase of AOCH. For this study, there are two main efficacy endpoints being evaluated. The primary efficacy endpoint is time to progression (TTP), where progression is defined as the first measurement time at least 7 days and up to 28 days after Baseline at which a 5-point or greater increase in MELD Score is recorded relative to Baseline MELD score. The secondary efficacy endpoint is the proportion of subjects who have not progressed (as defined in the primary endpoint) at 28 days following Baseline.

Inclusion and Exclusion Criteria

An eligible subject must meet ALL of the following criteria to be considered for this study:

- 1) Weight ≥ 40 kg; AND
- 2) Age $\geq 18 \leq 65$ years; AND
- 3) Documented evidence of chronic liver disease within the previous 4 weeks prior to the onset of the acute disease process; AND
- 4) Acute decompensation of chronic liver disease over the preceding 14 days; AND
- 5) MELD score between 18 and 32 (inclusive); AND
- 6) One or more of the following;
 - a. Encephalopathy of grade 2, 3 or 4 on the Westhaven scale (performed by physician); AND/OR
 - b. Renal dysfunction typical of type-1 hepato-renal syndrome, i.e., acute renal failure at study entry without evidence of chronic renal dysfunction (elevated serum creatinine (> 2.5 mg/dL) during the 1 to 6 months prior to study entry). Serum creatinine at study entry > 2.5 mg/dL does not exclude the subject from enrollment; AND/OR
 - c. Clinical diagnosis of Acute Alcoholic Hepatitis; AND
- 7) Subject or designated representative must provide Informed Consent.

There is a detailed list of exclusion criteria that a subject must not meet in order to be an eligible participant in this study. These include conditions, such as, decreased platelet levels, diagnosis of active sepsis, and evidence of major hemorrhage, to name a few. We encourage you to speak with the Principal Investigator at the local institution to further determine eligibility of potential candidates for ELAD[®] therapy.

Further Information

For more information, please contact Rob Ashley, Chief Operating Officer at (858) 673-6840. Also, please visit www.vitaltherapies.com or www.clinicaltrials.gov for additional information. A complete list of open and potential study centers can be found at www.clinicaltrials.gov.