A RANOMIZED, OPEN-Label, Multicenter, Controlled Study to Assess Safety and Efficacy of ELAD®, A Human Cell-Based Bio-artificial Liver Support System, in Subjects with Alcohol-Induced Liver Decompensation (AILD)

Rob A. Ashley*, Jan Stange2, Andrew J. Henry3, Zheng Li1
1Research & Development, 2Medical Affairs, 3Clinical Operations, Vital Therapies, Inc., San Diego, United States

BACKGROUND

Treatment options for patients with AILD are limited, leading to significant morbidity and mortality. ELAD® is designed to provide liver support continuously for up to 10 days to a subject with compromised liver function and allow time for the native liver to regenerate by circulating patient plasma through a hollow fiber cartridge containing metabolically-active, immortalized VTL C3A human liver cells.

STUDY OBJECTIVE

Based on preliminary findings from a subset of subjects with AILD enrolled in a prior Phase 2 study (VTI-206), the aim is to provide data on the safety and clinical utility of ELAD in a larger, prospectively-defined population with AILD. The primary endpoint will evaluate overall survival of subjects with AILD and the secondary objectives are to determine the clinical diagnosis of AILD up to at least Study Day 91.

RESULTS

Study power assumptions included defining a 90-day control survival rate of approximately 50% and a study treatment arm survival improvement of approximately 20%, consistent with findings from prior studies. According to the AAH-MELD calculator1 which was reflected in a 90-day survival of approximately 72%, also consistent with the MELD calculator (69%), irrespective of treatment arm (prednisolone, pentoxifylline, the combination or placebo).

CONCLUSIONS

Trial enrollment has proceeded in accordance with the anticipated timelines. Average age and MELD score at baseline are within the trial target ranges established during VTI-206. Baseline data characterize a group of subjects with alcohol-induced liver decompensation.

REFERENCES

1.MELD score and 90-day mortality rate for alcoholic hepatitis. MAYO clinic.
2.Results of the STOPAH Trial. AASLD. 2014.
3.Exploratory objectives are to evaluate the ability of ELAD to stabilize liver function, measured using the Model of End-stage Liver Disease (MELD)-based time ELAD to stabilize liver function, measured using the Table 1. Key inclusion/exclusion criteria

<table>
<thead>
<tr>
<th>Inclusion criteria</th>
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<tbody>
<tr>
<td>Age ≥ 18yrs</td>
<td>Childbirth during study period</td>
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<tr>
<td>MELD 20-36</td>
<td>Inability to understand and comply with protocol</td>
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<td>Not pregnant</td>
<td>Active anabolic steroid use</td>
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<tr>
<td>No history of acute alcoholic hepatitis</td>
<td>Active severe anemia (Hgb &lt; 8g/dl)</td>
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Eligibility requirements (Table 1) were established in order to replicate the AILD population in VTI-206. Target age based on the VTI-206 population is 45-55 and baseline target MELD is 27-29 for the current study. A total of 200 evaluable subjects meeting these requirements will be randomly assigned in a 1:1 ratio to receive either standard of care treatment for AILD plus treatment with the ELAD System (ELAD group) or standard of care of treatment for AILD alone (Control group). ELAD treatment will take place for a maximum of five 24-hour periods unless any of the discontinuation criteria are met. It was anticipated that enrollment would take approximately 2 years.

The first subject was enrolled in March 2013 and enrollment was completed in January 2015. A total of 203 subjects were enrolled in 40 clinical sites in the United States, Europe and Australia (Graph 1) and the top ten enrolleurs are listed in Table 2. Based on data captured as of February 10, 2015 in the electronic data capture system for the study, the investigated population mainly comprised white (86.5%) males (59.0%). The age ranged from 25 to 68 years (mean= 45.6 years, SD=10.0 years, n=202). Hepatic encephalopathy was observed in 46.6% subjects at enrollment (Table 3). Major baseline laboratory variables include: MELD (27.2±3.8, n=196), Maddrey (72.9±25.0, n=197), bilirubin (25.0±9.2 mg/dl, n=196), INR (2.0±0.5, n=196), creatinine (1.0±0.7 mg/dl, n=196), PT (22.4±5.2 seconds, n=198), ALT (61.8±42.3 IU/L, n=198), AST (134±73.8 IU/L, n=196), sodium (133.9±5.5 mmol/l, n=198), WBC (14.5±7.4 X10³/mm³, n=198), etc. (Table 4).

DISCUSSION

The study endpoints are primary effectiveness and safety. Subjects will be randomized 1:1 ratio to receive either standard of care treatment for AILD alone or treatment with the ELAD System (ELAD group). The primary endpoint will evaluate overall survival of subjects with AILD up to at least Study Day 91. Secondary objectives are to determine the clinical diagnosis of AILD up to at least Study Day 91, and to provide data on the safety and clinical utility of ELAD in a larger, prospectively-defined population with AILD. The 90-day survival rate of approximately 50% is consistent with findings from prior studies. According to the AAH-MELD calculator, a MELD of 27.2 translates to a 90-day survival rate of 49%. A recent study of sAAH subjects in the UK (the STOPAH trial) enrolled a less sick subject population (mean baseline MELD ~22) which was reflected in a 90-day survival of approximately 72%, also consistent with the MELD calculator (69%), irrespective of treatment arm (prednisolone, pentoxifylline, the combination or placebo).

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REFERENCES


Contact Information
Robert Ashley, MA
15010 Avenue of Science, Suite 200, San Diego, CA 92128
858-673-6480 phone, 858-673-6843 fax
ashley@vitaltherapies.com