ELAD® Cellular and System Performance Improvements

Brotherton, John2; He, Dar2; Asslani, Shapour2; Millis, Michael1

1. Dept of Surgery, University of Chicago, Chicago, IL, USA
2. Vital Therapies, Inc, San Diego, CA, USA

Abstract

One of the concerns with immortalized human hepatocytes has been the robustness of the metabolic pathways. As evidence mounted that the pathways expressed were dependent on the conditions the cells were exposed to, effort was placed on optimizing the metabolic function, by modifying the materials and conditions.

Methods

C3A cells were inoculated into improved polysulphone hollow fiber cartridges with 0.2 micron pores and allowed to grow to confluence. Oxygen delivery and culture media were optimized, with pH and temperature maintained at physiologic conditions. Standard metabolic assessments were performed and compared to the cartridges utilized in earlier Phase 1 and 2 clinical trials.

Results

Metabolic Activity of ELAD® Cartridges

<table>
<thead>
<tr>
<th>Metabolite</th>
<th>Phase 1 and 2 Cartridges</th>
<th>New Cartridges and Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Factor V (mg/d/cartridge)</td>
<td>0.056 ± 0.017 (n=25)</td>
<td>1.12 ± 0.83 (n=17)</td>
</tr>
<tr>
<td>Glucose Consumption (g/d/cartridge)</td>
<td>13.0 ± 1.8 (n=146)</td>
<td>17.6 ± 2.3 (n=111)</td>
</tr>
<tr>
<td>Lactate Production to Glucose Consumption Ratio</td>
<td>0.59 ± 0.04 (n=25)</td>
<td>0.38 ± 0.13 (n=111)</td>
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<tr>
<td>Urea Production (mg/d/cartridge)</td>
<td>N/A</td>
<td>88.5 ± 45.8 (n=89)</td>
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<tr>
<td>Albumin Production (mg/d/cartridge)</td>
<td>264.6 ± 85.3 (n=145)</td>
<td>365.2 ± 87.1 (n=109)</td>
</tr>
<tr>
<td>Transferrin Production (mg/d/cartridge)</td>
<td>86.8 ± 29.7 (n=163)</td>
<td>127.5 ± 36.9 (n=171)</td>
</tr>
<tr>
<td>Galactose Consumption (µmol/h/cartridge)</td>
<td>28.7 ± 5.1 (n=31)</td>
<td>41.6 ± 9.8 (n=6)</td>
</tr>
<tr>
<td>TGF-α Production (ng/d/cartridge)</td>
<td>50.3 ± 18.1 (n = 24)</td>
<td>485.7 ± 407.9 (n=16)</td>
</tr>
</tbody>
</table>

All Differences are statistically significant to the 0.001 level

Conclusion

The metabolic growth and maintenance conditions that the C3A cells are exposed to and the physical characteristics of the hollow fiber cartridge utilized significantly affect the metabolic repertoire of the cells. The improved metabolic characteristics may have significant affect on the level of metabolic support provided by the ELAD System. The new system with improved metabolic characteristics is currently in a randomized, multi-center clinical trial assessing the safety and efficacy of the ELAD System for acute decompensation of chronic liver disease.

Reference

Acute Liver Failure
Monday, November 5
3:00 - 4:30 PM Hynes, Room 302
MODERATORS: J. Eileen Hay, MD
Andres T. Blei, MD

3:00 PM #91
INTERIM RESULTS OF RANDOMIZED CONTROLLED TRIAL OF ELAD® IN ACUTE ON CHRONIC LIVER DISEASE
Zhong-Ping Duan1, Jing Zhang2, Shaojie Xin3, Ju Mei Chen4, Dar He5, John D. Brotherton5, Kameron Maxwell5, Michael Millis5
1Transplantation, University of Chicago, Chicago, IL, USA.
2Vital Therapies, Inc, San Diego, CA, USA.
3Beijing Youan Hospital, Beijing, China.
4302 Military Hospital, Beijing, China.