3-year follow up of acute-on-chronic liver failure (ACLF) subjects in a randomized, controlled, multicenter trial of the ELAD® Bioartificial Liver Support System in 49 Chinese subjects reveals significant transplant-free survival (TFS) benefit

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ABSTRACT

Background: Patients with ACLF suffer significant morbidity and mortality. ELAD circulates patient plasma through hollow fiber cartridges containing metabolically active, immortalized C3A human liver cells of hepatoblastoma origin. A hypothetical risk of late tumor development exists.
Aim: Determine 3-year TFS and tumor incidence in a controlled study of safety and efficacy of ELAD in ACLF subjects in China.
Methods: Subjects were enrolled in a randomized (2:1), open label, controlled trial of 49 subjects with chronic HBV or HCV and a current episode of acute decompensation at 2 Chinese liver disease centers. After randomization subjects underwent plasma exchange then either continuous ELAD treatment or standard of care until recovery. Subjects or their families were contacted 3 years following enrollment of the last subject and consented. Survivors underwent a cancer screen (AFP, ultrasound) and physical exam in accord with a questionnaire.
Results: Of 49 subjects enrolled, 84-day TFS was 21/32(65.6%) in the ELAD group vs 7/17 (41.1%) in controls. 3 year TFS was 14/32 (43.8%) in the ELAD group vs 3/17 (17.6%) in controls (p=0.045, log-rank test). Of 84-day survivors, 2/21 (9.5%) ELAD and 2/7 (28.6%) controls died, 1/21 (4.8%) ELAD and 0/7 controls were transplanted and 4/21 (19.0%) ELAD and 2/7 (28.6%) controls were lost to follow-up at 3 years. No death or transplant was attributed to tumor (either hepatic or of any other origin) and no survivors had evidence of tumor. There was no difference in survival or transplant patterns between the two sites.
Conclusion: 3 year follow up of subjects enrolled in a clinical trial of ELAD in ACLF patients in China confirmed that ELAD confers a statistically significant 3-year transplant-free survival advantage compared with standard of care alone. There was no evidence of an increased risk of tumor formation in this patient population.

OBJECTIVE

Determine 3-year transplant-free survival (TFS) and tumor incidence in a controlled safety and efficacy study of ELAD in ACLF subjects in China

HYPOTHESIS

- **ELAD does not increase the tumor incidence over a 3-year follow up in subjects with ACLF relative to standard of care (SOC)**
- **TFS improvements previously reported in subjects with ACLF treated with ELAD at 84 days follow up would be maintained at 3 years relative to SOC**

METHODS

Randomized, concurrent controlled clinical trial at two Chinese liver disease centers

Key inclusion criteria:

- **acute on chronic liver failure due to various causes; e.g., virus, alcohol, drug or congenital & metabolic disease**
- **total bilirubin (TBil)>5x ULN, or daily increase of TBil >1 mg/dL (17.1 μmol/L)**
- **INR >1.6**

Key exclusion criteria:

- **grade III or IV hepatoencephalopathy**
- **platelets <50×10^9/L**
- **creatinine >1.5 mg/mL**
- **INR ≥ 4.0**

Procedures:

- **Plasma exchange**
- **Continuous veno-venous hemofiltration**
- **Random assignment to either ELAD or SOC**

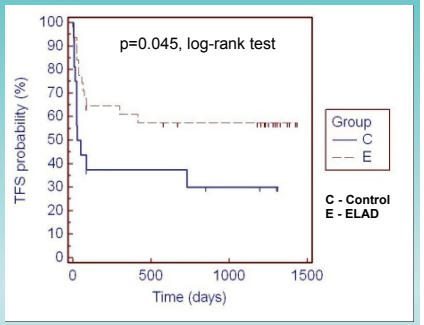
Follow up (3 years):

- **Subjects consented**
- **Cancer screen**
  - **AFP**
  - **Ultrasound**
- **Physical exam**
  - **Questionnaire**

RESULTS

Transplant-Free Survival

	ELAD (N=32)	Control (N=17)
TFS (84 day)	21/32 65.6%	7/17 41.1%
Of the transplant-free survivors at 84 days, at 3 year follow up:		
Lost	4/21 19%	2/7 28.6%
Death	2/21 9.5%	2/7 28.6%
Transplant	1/21 4.8%	0/7 0.0%
TFS (overall)	14/32 43.8%	3/17 17.6%
TFS (84d – 3 years)	14/21 66.6%	3/7 42.9%



Tumor Screen

	ELAD (N=21)	Control (N=7)
Tumor related deaths	0	0
Tumor related transplant	0	0
Evidence of tumor in survivors	0	0

CONCLUSIONS

Three year follow up of ACLF subjects enrolled in a randomized, controlled multicenter trial of ELAD:

- **did not reveal an increased incidence of tumors**
- **demonstrated a statistically significant TFS advantage in ELAD treated subjects compared with SOC**

These data confirm previous reports of a significant 84-day TFS advantage for ELAD treated ACLF subjects compared with SOC

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