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CITATION: “Prospective, Randomized, Multi-Center, Controlled Trial of a Bioartificial Liver in Treating Acute Liver Failure,” *Annals of Surgery*, May 2004.

HIGHLIGHTS: A bioartificial liver developed by researchers at Cedars-Sinai Medical Center reduced mortality significantly among patients suffering from acute liver failure, according to a clinical trial conducted at 20 centers in the United States and Europe. With a complex filtering system that incorporates liver cells from pigs, the bioartificial liver cleanses and nourishes the blood to prolong life while an injured liver recuperates or a donor organ becomes available for transplantation. Study results are published in the May issue of *Annals of Surgery*.

MAJOR STUDY: BIOARTIFICIAL LIVER REDUCES MORTALITY BY 44% IN ACUTE LIVER-FAILURE PATIENTS

LOS ANGELES (APRIL 22, 2004) – In a major study conducted at 20 centers in the United States and Europe, a bioartificial liver developed by researchers at Cedars-Sinai Medical Center reduced mortality significantly among patients suffering from acute liver failure, the dramatic loss of liver function that can cause death in days or even hours. Study results are published in the May issue of *Annals of Surgery*.

This is the first large-scale, prospective, randomized, multi-center trial examining the effectiveness of any artificial liver support. Currently, standard treatment consists of intensive, supportive care intended to keep patients alive long enough that the liver might recover spontaneously or a donor organ will become available for transplantation.

Acute liver failure is diagnosed when a massive loss of hepatic cells causes severe liver dysfunction and life-threatening complications within six months of the onset of symptoms. When this dysfunction occurs within the first eight weeks after onset, liver failure is termed “fulminant.” When it occurs in the period between eight weeks and six months, it is “subfulminant” (or late-onset). In either case, few patients survive the resulting fluid buildup in the brain, catastrophic bacterial infections, multi-organ failure, blood-clotting abnormalities, respiratory problems, kidney failure or other potential complications. It is estimated, in fact, that up to 80 percent of patients will die unless they receive a liver transplant.

In the United States, the causes of many cases of acute liver failure are never identified, although precipitating factors can include toxic poisoning, medication interactions or overdoses, metabolic disorders, and some types of viral hepatitis.

(more)

Achilles A. Demetriou, MD, PhD, Chairman of Surgery at Cedars-Sinai and the study's principal investigator, has been pursuing treatments for acute liver diseases since 1976 when he began studying liver cells at the National Institutes of Health. He continued his research at Vanderbilt University, coming to Cedars-Sinai in 1992 to launch the country's first unit devoted to managing massive acute liver failure.

The study included 147 patients who suffered from fulminant/subfulminant hepatic failure and 24 patients whose livers had failed after transplantation. Of the 171 total patients, 85 received BAL treatment, while 86 received standard supportive care.

For the entire patient population, survival at 30 days was 71 percent among the BAL group, compared with 62 percent for those receiving traditional care. Analyzing results among only the 147 patients with fulminant/subfulminant hepatic failure, the researchers found that the BAL provided a 44 percent reduction in mortality.

During a treatment, blood is drawn from a vein through a catheter. Blood plasma is separated from the serum and pumped through a charcoal column and an oxygenator before it reaches the bioreactor – a tube-shaped device containing a fiber membrane and 7 billion liver cells from pigs. These cells are isolated, cryopreserved (frozen) and thawed according to techniques originally developed by the Cedars-Sinai researchers.

“The blood is removed at a fixed rate, detoxified and treated in the various components of the bioartificial liver, reconstituted, and returned to the patient at the same rate at which it is being removed,” said Dr. Demetriou. “Just before the patient is treated, the pig liver cells are thawed, reactivated and attached to small beads that serve as a scaffold for the cells. We put the cells and beads into the cartridge, and when the patient's plasma flows through the fibers, the pig liver cells detoxify it and replace missing nutrients.”

Each treatment is completed in about six hours, and the benefits last about 24 hours. In most cases of acute liver failure, a series of treatments may need to continue for only a few days or several weeks. “Typically, within that time the patient's condition is going to improve because his or her own liver kicks in or a liver will be available for transplantation,” Dr. Demetriou said.

The study was funded by Circe Biomedical Inc.

Cedars-Sinai is one of the largest nonprofit academic medical centers in the Western United States. For the fifth straight two-year period, it has been named Southern California's gold standard in health care in an independent survey. Cedars-Sinai is internationally renowned for its diagnostic and treatment capabilities and its broad spectrum of programs and services, as well as breakthroughs in biomedical research and superlative medical education. The Medical Center ranks among the top 10 non-university hospitals in the nation for its research activities.

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