Acute-on-chronic liver failure: extracorporeal liver assist devices
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Purpose of review
Acute-on-chronic liver failure (ACLF), a syndrome precipitated by acute liver injury in patients with advanced cirrhosis, is associated with multorgan dysfunction and high rates of mortality. Liver support systems have been developed in an attempt to improve survival of patients with ACLF by providing a bridge until recovery of the native liver function.

Recent findings
Nonbiological devices such as molecular adsorbent recirculating system (MARS) and fractionated plasma separation and adsorption (Prometheus) are effective in improving severe hepatic encephalopathy and cholestasis, have good safety and tolerability profiles and are frequently employed in patients with ACLD; however, randomized controlled trials (RCTs) failed to show improvement in survival. Biologic devices that incorporate hepatic cells in bioreactors are also under development. Recent data from pilot studies suggested improvement in survival rates in some groups of patients with ACLF; however, their effect on patient survival in RCT is still unknown.

Summary
Liver support systems are safe and well tolerated when used in management of patients with ACLF. Their use should continue in controlled clinical trials to explore their role in bridging patients to liver transplantation or recovery in well defined patient groups.

Keywords
acute-on-chronic liver failure, artificial liver support, extracorporeal liver assist device, liver support systems, molecular adsorbent recirculating system, Prometheus

Introduction
The liver is a complex multifunctional organ necessary for human organism survival. Digestive, immune, metabolic, synthetic and excretory functions of the liver play a crucial role in maintaining function of other organs and body homeostasis [1]. It has major immunologic functions and its role in inflammation is being further elucidated. Although the liver’s functional reserve and regenerative capacity are great, these could be hindered in the face of severe acute liver injury [1].

Cirrhosis represents an end-stage of progressive hepatic fibrosis accompanied by regenerative nodule formation and inflammation in response to chronic and long-standing injury. Cirrhosis and its complications are a growing problem worldwide. It is the fifth leading cause of death in 45–49-year-olds and the 10th leading cause of death in people over the age of 60 worldwide [2]. According to a WHO report, 800 000 people died from cirrhosis in 2004, surpassing the mortality from colorectal cancer [3]. The most common causes of cirrhosis in the United States are hepatitis C virus (HCV), 26%, alcoholic liver disease, 21%, a combination of both, 18%, cryptogenic cirrhosis, 18%, hepatitis B virus (HBV), 15%, and various other causes of chronic liver disease, 5% [4]. Recently, Davis et al. [5*] forecasted that there will be significant increases in the number of Americans with cirrhosis due to chronic HCV, with an estimated prevalence reaching 1 million individuals by 2020. Similarly, as the prevalence of obesity rises in the United States, nonalcoholic fatty liver disease is increasingly recognized as an important cause of chronic liver disease, and many cases of cryptogenic cirrhosis are now attributed to nonalcoholic steatohepatitis [6*].

To assess severity of hepatic dysfunction and probability of survival in cirrhotic patients, the Child–Turcotte–Pugh score (CTPS) was introduced in 1973. The patient is assessed based on signs of deterioration of major hepatic functions: serum albumin concentration and prothrombin time or INR (synthetic function), bilirubin (excretory), encephalopathy (detoxifying), and presence of ascites (development of portal hypertension) [7]. The 1-year mortality rate in patients with CTPS greater than 10 is close to 50% [4]. In addition, the Model for End-Stage Liver Disease (MELD) score has been used for estimation of the severity of hepatic dysfunction and the
need for transplant. It incorporates serum bilirubin and creatinine levels and INR [MELD = 3.78 (ln serum bilirubin [mg/dl]) + 11.2 (ln INR) + 9.57 (ln serum creatinine [mg/dl]) + 6.43]. Use of hemodialysis is accounted for in the calculation by assigning a creatinine level of 4 (http://www.unos.org/docs/MELD_PELD_Calculator_Documentation.pdf). The MELD score is used for organ allocation based on assessment of severity of hepatic decompensation and predicted mortality in a given patient. Estimated 3-month mortality is associated with the following MELD scores: MELD score of less than 9, 2.9% mortality; MELD score of 10–19, 7.7% mortality; MELD score of 20–29, 23.5% mortality; MELD score of 30–39, 60% mortality; and MELD score of greater than 40, 81% mortality.

**Acute-on-chronic liver failure**

Although patients with cirrhosis may exhibit sufficient liver function for a long time, an acute insult to the organ in the setting of advanced fibrosis and low residual function may lead to hepatic decompensation (Fig. 1). These patients are diagnosed with acute-on-chronic liver failure (ACLF). Early intervention including removal of the injurious agent and supportive care may stabilize hepatic function and help patients to return to their baseline functional status. The recovery of hepatic function may still be possible, but it requires time and supportive care. However, in a large number of patients despite all efforts further deterioration of liver function often accompanied by multiorgan dysfunction occurs putting them at risk of death. Liver transplantation is the only option for this subset of patients, but candidates need to be clinically stable at the time of surgery to survive. In addition, liver transplantation is limited by...

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**Key points**

- Acute-on-chronic liver failure is a clinical state associated with very high mortality.
- Early detection of liver decompensation in patients with cirrhosis and identification of the precipitating cause of decompensation are essential for adequate early intervention to reverse the decompensation.
- Patients who fail standard medical approaches could benefit from artificial liver support (ALS), particularly in cases of hepatic encephalopathy and progressive cholestasis.
- Although ALS so far fails to improve survival, well designed multicenter clinical trials should continue in well defined subsets of patients and with standardized realistic outcome measures.
- Success in defining which patients will benefit from ALS will pose the next challenge as will determining which group of patients are candidates for bioartificial liver systems.
- Bioartificial liver systems will have the burden of improving survival or prolonging the wait on the liver transplant list.

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**Figure 1** Patients with compensated cirrhosis, decompensate as a result of disease progression or new insults
organ scarcity. In the United States, the United Network for Organ Sharing (UNOS) maintains the list of patients in need of a transplant. When a donor liver becomes available, potential appropriate recipients are selected based on the MELD score. Currently, approximately 15% of patients on the U.S. liver transplant waiting list die before they are able to receive a liver due to insufficient donor organ availability and progressive liver failure [4]. To overcome the organ shortage, new surgical approaches have been developed, including split liver transplantation, living donor transplantation, donation after cardiac death (DCD) and auxiliary transplantation [8]. However, some patients are removed from the waiting list due to ACLF, multiorgan failure or sepsis. New concepts are continuously being developed in an attempt to both prolong life in decompensated patients until they recover their liver cell function and to maintain their status as viable candidates for liver transplantation [9]. Despite significant progress in this field in the last decade, the best methods to attain this goal have not been determined nor is it yet clear precisely which liver functions are most critical for survival in this setting. Multiple liver support systems have been under development for the last 50 years. The ultimate goal of these systems is to extracorporally substitute liver functions, such as detoxification, excretion and synthesis, at the time of acute hepatic injury while allowing the native liver to recover or for a transplant organ to become available [10].

There are three major types of liver support systems: nonbiological, biological and a combination of the two (Table 1) [11–21].

Nonbiological or artificial systems are dialysis systems designed to provide detoxification and purification only. They remove toxic substances from the blood stream and have no cells in their working structure [10]. Examples of these systems are molecular adsorbent recirculating system (MARS, Gambro GmbH, Hechingen, Germany), the fractionated plasma separation and adsorption system (FPSA, Prometheus, Fresenius AG, Bad Homburg, Germany), single-pass albumin dialysis (SPAD) and selective plasma filtration system therapy (SEPET, Arbios Systems Inc., New York, New York, USA).

Biological or bioartificial liver (BAL) systems are cell-based dialysis techniques that utilize porcine or human hepatocytes, loaded into hollow-fiber bioreactors that are perfused with the patient’s blood or plasma to provide liver-specific functions including synthetic (proteins and clotting factors), regulatory (hormones), immunologic function and biotransformation. The development of an effective bioartificial liver that emulates a functional liver has been challenging due to the complexity of liver structure and the diversity of hepatocyte functions. Challenges include selecting the sources of hepatocytes for the bioreactor; the stabilization of these primary hepatocytes in the bioreactor to maintain morphology, differentiation and function; and the design of the bioreactor, which requires adequate bidirectional mass transport, and cell viability to perform liver functions. Issues of safety with regard to infection and oncogenesis, as well as high cost are major concerns of these systems, which are considered as yet to be experimental [22].

Finally, the third type of liver support system is a hybrid that incorporates features of both nonbiological and biological devices in order to better mimic hepatocyte functions and permit dialysis of toxins and bile components produced in the bioreactor, as all biological devices lack a compartment for biliary excretion [23, 24].

**Role of nonbiological devices in acute-on-chronic liver failure**

Nonbiological devices are simple dialysis systems that provide a means to remove water-soluble and albumin-bound toxins from the patient’s plasma. Their use has increased since the introduction of extracorporeal albumin dialysis (ECAD), which involves dialyzing the patient’s blood against an albumin-containing dialysate in order to remove albumin-bound and water-soluble molecules [25]. Examples of ECAD devices are the MARS and SPAD systems.

Albumin dialysis or MARS (Fig. 2) was introduced in 1993 and has gained popularity [11]. Since its introduction, it has been employed in over 9000 patients, but very few randomized controlled trials (RCTs) have been conducted and published. A patient’s blood is dialyzed against a higher concentration albumin solution employing a semipermeable membrane and then the waste product-rich albumin solution is passed through a second dialyzer to remove water-soluble byproducts. Subsequently, albumin-bound substances are removed by filtration through a charcoal filter and anion exchanger. Regenerated albumin continues to recirculate. The efficacy of removal of albumin-bound substances depends on their affinity for albumin-binding sites and albumin concentration [26]. Safe and well tolerated, MARS treatments have been shown to improve systemic hemodynamics probably by decreasing the concentration of

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**Table 1 Liver support systems**

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<th>Nonbiological</th>
<th>Biological</th>
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<td>SEPET [14]</td>
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AMC-BAL, AMC-Bioartificial Liver; BLSS, Bioartificial Liver Support System; MARS, molecular adsorbent recirculating system; MELS, Modular Extracorporeal Liver Support; RFB, Radial Flow Bioreactor; TECA-HALSS, TECA-Hybrid Artificial Liver Support System.
circulating vasoactive substances, ameliorating hyperdynamic circulation and increasing the mean arterial pressure in patients with ACLF [27,28]. MARS has been proven effective in removing more water-soluble and albumin-bound substances when compared to conventional hemodialysis (Table 2) [29*]. It has also been shown to decrease portal pressure, improve renal blood flow and remove ammonia to enhance cerebral perfusion pressure [30,31]. Clinically, MARS has been successfully used for patients with hepatic decompensation, who presented with hepatic encephalopathy, hepatorenal syndrome and progressive hyperbilirubinemia [31]. MARS demonstrated substantial superiority in the treatment of severe hepatic encephalopathy (grade 3 and 4) when compared with standard of care in RCTs [32]. The proposed effects of albumin dialysis in patients with hepatic encephalopathy are summarized below [33–40]:

1. Ammonia and aromatic amino acids are removed.
2. Other hepatic encephalopathy-related albumin-bound and nonbound molecules and endozepines are removed.
3. Serum albumin-binding sites and albumin-binding capacity are increased.
4. Oxidative stress-mediated damage to albumin is restored.
5. Hemodynamics and organ perfusion are improved.
6. Endogenous vasoactive substances are changed.
7. Inflammatory mediators and cerebral hemodynamics are modulated.

MARS has also shown efficacy in reducing serum urea and creatinine concentration and improving urine output in patients with hepatorenal syndrome (HRS) [41]. In some studies, HRS resolution and improvement of short-term mortality were achieved; however, these effects were not reproduced in other trials [31,42*].

Cholestasis and hyperbilirubinemia are often seen in patients with ACLF and may be severe. In high concentrations, bile acids may induce apoptosis and cell necrosis of hepatocytes and retard hepatic regeneration. Clinically, cholestasis presents with pruritis, renal and pulmonary vascular injury, and hemodynamic changes. Multiple studies have demonstrated the efficacy of albumin dialysis in decreasing total bile acid pool and bilirubin concentration, providing relief of the clinical manifestations of cholestasis [43,44]. MARS treatment could be a useful tool in facilitating hepatic recovery in patients with severe drug-induced liver injury with features of cholestasis, posttransplant cholestasis due to graft dysfunction, and in liver failure patients awaiting transplantation [45,46,47*]. Albumin dialysis is also effective in improving intractable pruritis from severe cholestasis in some patients with cholestatic conditions [48,49*].
Previously, MARS was found to provide short-term survival benefit in a few RCTs [33,41]. However, results of a recent multicenter RCT reported as an abstract that compared MARS therapy and standard medical therapy (SMT) did not demonstrate a significant difference in mortality. Nevertheless, in this study, MARS treatment was effective in reducing encephalopathy grade and improving hemodynamic parameters while maintaining a good safety profile (RELIEF study) [50]. This multicenter study included 189 patients with ACLF complicated with either HRS type 1, hepatic encephalopathy grade 2 or higher, or worsening hyperbilirubinemia. Patients were randomized to receive either MARS in combination with SMT or SMT alone. Patients in the MARS group demonstrated significant improvement in serum bilirubin, creatinine and hepatic encephalopathy compared with the SMT group. Treatment was well tolerated, but no overall survival benefit after 28 days of therapy was demonstrated in the MARS group when compared with SMT alone (28-day mortality was 40% in SMT versus 41.2% in MARS, log rank \( P = 0.88 \)).

Despite this lack of advantage in overall survival benefit when compared with standard of care therapy, MARS had short-term mortality benefit in a subgroup of patients who experienced early improvement of hepatic encephalopathy, HRS and cholestasis [50]. In addition, previous pilot studies reported improved survival with MARS therapy in patients with toxic hepatitis, alcohol-induced ACLF and in posttransplant graft failure [51–53]. Hence, use of MARS as a bridge to transplantation should be explored further in RCTs.

**Single-pass albumin dialysis**

Similar to MARS, SPAD is a nonbiologic liver support system designed to remove protein-bound and watersoluble substances from blood (Fig. 3). It entails addition of albumin to a hemodialysis solution achieving 5% concentration and use of a high flux albumin-impermeable dialyzer. As with MARS, the efficacy of removal of these molecules depends on their affinity for protein-binding sites. For example, bile salts are removed more effectively than bilirubin. With SPAD, clearance of bilirubin can be dramatically improved by increasing albumin concentration, but at significant cost [54]. Studies comparing MARS and SPAD concluded that both methods are similar in their effectiveness of clearance of bile salts, ammonia, urea, creatinine and bilirubin [12]. No RCTs have been conducted.

**Fractional plasma separation adsorption and dialysis**

Prometheus liver support therapy utilizes a plasma separation technique combined with adsorption [55] (Fig. 4). The patient’s blood is circulated through the specialized membrane (AlbuFlow), which allows separation of blood cells and large proteins from plasma and molecules that are less than 250 kDa in size. Filtered plasma is circulated through two columns of adsorbents, neutral resin and an anion-exchange resin. The patients’ blood cell filtrate and plasma are combined and dialyzed via a high-flux dialyzer to remove water-soluble molecules before returning to the patient [26,13,56].

The clinical experience with Prometheus has demonstrated good safety and tolerability in patients with ACLF. In numerous comparative pilot studies with MARS, Prometheus showed effectiveness of FPSA in removing bile acids, bilirubin, ammonia, urea, creatinine and cytokines exceeding that of the MARS system in

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**Figure 3 Single pass albumin dialysis**

SPAD: single pass albumin dialysis is a form of extracorporeal albumin dialysis (ECAD). It involves adding albumin to standard dialysis solution, achieving an albumin concentration of 4–5%. The membrane used is a high-flux dialysis membrane which allows molecules up to 30 kDa to pass through [54].

**Figure 4 Prometheus**

Prometheus: fractional plasma separation adsorption and dialysis. It involves filtration of plasma and albumin through a membrane (AlbuFlow), which allows molecules up to 250 kDa to filter through. The filtrate is then passed over neutral resin and anion exchange resin, before it returns back to the blood circuit. The blood is then dialysed in standard fashion before it returns back to the patient [13].
some studies [55]. This improved efficiency may be explained by differences in solute transport in these systems: in MARS, solutes have to separate from the patient’s albumin in order to diffuse across an albumin-impregnated membrane; in Prometheus, molecules bound to the patient’s albumin pass through the adsorber by diffusion and convection and are directly filtered into the secondary circuit. Differences in clearance of watersoluble substances may be explained by differences in flow rate in the two systems [55]. However, the improvement in systemic hemodynamics seen with MARS was not observed with the Prometheus [57]. In addition, Prometheus requires consistent use of anticoagulants to prevent clotting of the system more than in MARS. Both heparin and citrate have been used safely during Prometheus therapy; however, addition of prostaglandins did not decrease the risk of circuit clotting [57,58].

Recently, a RCT based in 10 European centers (HELIOS study) evaluated the survival benefit of FPSA in patients with ACLF. The data were presented at the Annual Meeting of European Association for Study of Liver in April of 2010. In this study, 145 matched patients with ACLF were randomized to either standard medical therapy (SMT) alone or in conjunction with FPSA. The mean MELD score for these patients was 27 ± 10 and Child–Pugh score was 12 ± 1. In the FPSA group, patients received eight to 11 treatments in the first 3 weeks of the study. Therapy was safe and well tolerated. There was no overall statistically significant mortality benefit at 28 days (66% in SMT + FPSA versus 63% in SMT $P = 0.7$) [59**]. However, the study reported significant survival benefit in patients with HRS type 1 ($P = 0.04$) and in patients with MELD higher than 30 ($P = 0.02$). Details of these studies are not yet published.

**Selective plasma filtration therapy**

SEPET utilizes hemodialysis hardware and a hollow-fiber filter with a membrane pore size permitting passage of molecules with molecular weight less than 100 kDa (Fig. 5). Hence, it preserves immunoglobulins, complement proteins, most clotting factors and hepatocyte growth factor (HGF). Due to the membrane pore size, part of the patient’s albumin is lost during treatment and needs to be replaced after its completion. The filtered substances include ammonia, aromatic amino acids, bile acids, bilirubin, mercaptans, some proinflammatory cytokines, tumor necrosis factor α and endotoxin [60]. The removed fluid is replaced by fresh frozen plasma, albumin and an electrolyte solution. In animal models with fulminant hepatic failure, SEPET improved survival and hepatic regeneration [61]. The SEPET device safety-trial confirmed its safety and tolerability and its efficacy in improving hepatic encephalopathy [14]; however, this liver assist device remains under development.

**Bioartificial assist devices**

The lack of survival benefit of artificial liver support (ALS) systems in patients with ACLF underscores the importance of developing BALs with the abilities to improve survival in this class of patients. Numerous BAL devices have been under investigation for over 50 years (Table 1). However, the clinical experience with BAL in patients with ACLF is still very limited [62]. In animal models of fulminant liver failure, the majority of bioartificial liver assist devices demonstrated efficacy in providing liver cell
function and allowed the animal to survive the event [15]. In patients with ACLF, very few biological devices had been in use and minimal data are available.

**Extracorporeal liver assist device**

ELAD (Vital Therapies Inc.) is a BAL device utilizing a conventional hollow-fiber bioreactor populated with an immortalized human hepatocyte cell line. The device is comprised of hollow fibers arranged in four cartridges and containing 440 g of human hepatocytes. When the patient’s plasma is perfused through the fibers, two-way transfer of metabolites occurs, allowing metabolism of toxins and synthesis of essential hepatocyte-specific substances, emulating liver function. The functional hepatocytes were able to remove a number of toxins accumulating in patients with liver failure and produce liver-specific proteins such as albumin, transferin, C3 complement, factor V, VII, TGF-α and HGF [63]. Efficacy of ELAD in supporting patients with ACLF has been investigated in two clinical trials.

The first trial was a pilot study from China that evaluated the use of ELAD in 49 patients with ACLF [64]. Thirty-two patients received ELAD and SMT, whereas 17 patients received SMT alone. Patients with severe hepatic encephalopathy (grade 3 and 4), infections and any other organ failure were excluded. MELD scores were 24/7.0, and 80% of the patients had HBV-related liver decompensation. Patients in the ELAD arm received a mean of 68±18 h of liver support. Transplant-free survival at day 28 was 81.2% in the ELAD group versus 47.1% in the SMT group (P = 0.14). During treatment, an increase in MELD score by five points or more predicted transplant requirement or death. The long-term follow-up of the same cohort showed maintenance of transplant-free survival in the ELAD group after 3 years [65**].

The second study was a phase II US pilot study of patients with ACLF with MELD scores 24 or more and severe hepatic encephalopathy (grade 3 and 4) or HRS type 1 [66**]. Eighteen patients were randomized to ELAD in combination with SMT (n = 14) or SMT alone (n = 4). The mean MELD scores in the two groups were 37 and 42, respectively. Survival at 30 days was 46 and 50%, respectively, whereas transplant-free survival for the same duration was 23 and 0%, respectively. The average length of ELAD treatment was 122.8±21.7 h. Treatment was safe and well tolerated. The study results helped in planning an ongoing multicenter international clinical trial (Silver Trial), which is still recruiting patients.

**Conclusion**

In summary, continuous increase in the number of patients with cirrhosis due to chronic viral hepatitis,
alcohol and increasing prevalence of nonalcoholic fatty liver disease will lead to an increased burden of ACLF. Management of these patients will continue to pose a challenge for clinicians in an era of liver transplantation limited by severe donor organ shortage. ALS could be offered to patients with acute decompensation when standard therapy is failing. Determination of which patients would most benefit from such therapies is not yet known and is essential for the planning of future clinical trials (Fig. 6). The data from recent studies evaluating use of nonbiological liver assist devices are helpful in determining which patients would benefit from such support systems and in identifying patients who will need more advanced liver support than detoxification alone and who would benefit from use of biologic liver assist devices. These devices were well tolerated and the safety is equivalent to dialysis procedures except for more thrombocytopenia and risk of bleeding.

Although effective in improving severe hepatic encephalopathy, hemodynamic parameters, and cholestasis, nonbiological devices (MARS, Prometheus) did not impact overall survival in patients with ACLD. These devices should be assessed for their ability to bridge patients to liver transplantation in RCTs in well defined patient groups. The limitations seen with nonbiological devices underscore the importance of developing biological and hybrid treatment modalities, which could improve survival and provide better bridging therapy while awaiting liver transplant than nonbiological devices currently provide. We believe that biological devices should target those patients who fail nonbiological liver support. Until more data come forth, use of currently available liver assist devices should continue in clinical trials. More controlled randomized studies are needed to determine which subsets of patients with ACLF would benefit the most from each type of liver support devices, when the most optimal time is for initiation of such therapy and what the best duration of treatment is.

Acknowledgement
To the RELIEF and HELIOS study groups for providing the data presented at the EASL 2010. For Vital Therapies Inc. for providing summary of data presented at EASL 2010 and AASLD 2010.

References and recommended reading
Papers of particular interest, published within the annual period of review, have been highlighted as:
• of special interest
•• of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (pp. 209–210).


7. Potential effect of weight and BMI on progression of liver disease.


10. Outcome of liver transplantation for the different etiologies of ACLF.


30. Summary of the published experience of albumin dialysis using the MARS device.

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42 Wong F, Raina N, Richardson R. Molecular adsorbent recirculating system is ineffective in the management of type 1 hepatorenal syndrome in patients with cirrhosis with ascites who have failed vasoconstrictor treatment. Gut 2010; 59:1081–1086.
Positive effects of albumin dialysis on post-transplant graft dysfunction.
Effectiveness of albumin dialysis in ameliorating intractable prurititis.
RCT of the effects of MARS therapy on survival of patients with ACLF. A European study.
RCT of the effects of Prometheus on survival of patients with ACLF. An European trial.
65 Duan Z, Xin S, Zhang J, et al. 3-year followup of acute-on-chronic liver failure (AOCFL) subjects in a randomized, controlled multicenter trial of the ELAD bioartifical liver support system in 49 Chinese subjects reveals significant transplant-free survival (TFS) benefit. Hepatology 2010; 52:1089A.
Pilot trial of ELAD in patients with mild forms of ACLF.
Pilot trial of ELAD in patients with advanced forms of ACLF.