Indications for artificial liver support systems

P. Angeli
Dept. of Clinical and Experimental Medicine
University of Padova

13th AISF Pre-Meeting Course
“Difficult Clinical Issue in Hepatology”

Rome 23rd-26th, 2011
Artificial and bioartificial support systems for liver failure

Potential indications

- Acute liver failure (ALF)
- Acute on chronic liver failure (ACLF)
- Other forms of hepatic failure
Artificial and bioartificial support systems for liver failure

ALF or ACLF

Optimal medical care / Liver support systems

Recovery of liver function
Liver transplantation

Recovery/Survival
Artificial and bioartificial support systems for liver failure

Support system versus standard medical therapy: adverse effects

**BLEEDING**
- Hughes 1994 (Biological-DT)
- Kramer 1998 (Biological-DT)
- Ellis 1999 (Biological-DT)
- Hellis 1996 (ELAD)
- Mitzner 2000 (MARS)
- Heemann 2001 (MARS)

**SUBTOTAL**

**INFECTION**
- Hellis 1996 (ELAD)

**COAGULOPHATY**
- Heemann 2001 (MARS)

**TOTAL**

Favour experimental | Favour control
---|---
0.3 | 0.2 | 1 | 5 | 10

P = N.S.

*The Cochrane Database of Systematic Reviews 2004; 1:CD003628*
Artificial and bioartificial support systems for liver failure

Support system versus standard medical therapy: mortality

Redeker 1973 (Whole Blood Exchange)
O Grady 1988 (Charcoal haemotrasfusion)
He 2000 (Plasma exchange and haemoperfusion)
Hughes 1994 (Biological-DT)
Mazariegos 1997 (Biological-DT)
Kramer 1998 (Biological-DT)
Wilkinson 1998 (Biological-DT)
Ellis 1999 (Biological-DT)
Mitzner 2000 (MARS)
Heeman 2001 (MARS)
Hellis 1996 (ELAD)
Stevens 2001 (Hepat-assist)

Favour experimental P = N.S. Favour control

P = N.S.

The Cochrane Database of Systematic Reviews 2004; 1:CD003628
Artificial and bioartificial support systems for liver failure

Support system versus standard medical therapy: bridging to transplantation

Mazariegos 1997 (Biological-DT)
Kramer 1998 (Biological-DT)
Wilkinson 1998 (Biological-DT)
Ellis 1999 (Biological-DT)

P = N.S.

The Cochrane Database of Systematic Reviews 2004; 1: CD003628
Artificial and bioartificial support systems for liver failure

Support system versus standard medical therapy: the Cochrane Hepato-Biliary Group Metanalysis

**Inherent potential bias**

- Two among the included trials were performed in the 70s and 80s.
- No sample calculation in all but one included trials.
- Patients with different type of liver failure were included, ALF as well as ACLF.
- Support systems with quite different modalities of action were considered.
- Limited number of predefined subgroup analyses were performed.
Artificial systems removal of potential toxins

<table>
<thead>
<tr>
<th></th>
<th>High flux Dialysis</th>
<th>Coated Charcoal</th>
<th>20 % albumin solution (MARS)</th>
<th>Prometheus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ammonia</td>
<td>++</td>
<td>-</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Aromatic aminoacids</td>
<td>++</td>
<td>+</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Mercaptans</td>
<td>-</td>
<td>+</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Bilirubin</td>
<td>+/-</td>
<td>-</td>
<td>++</td>
<td>+++</td>
</tr>
<tr>
<td>Bile acids</td>
<td>+/-</td>
<td>-</td>
<td>++</td>
<td>+++</td>
</tr>
<tr>
<td>Cytokines</td>
<td>-</td>
<td>-</td>
<td>+/-</td>
<td>+/-</td>
</tr>
<tr>
<td>Nitric oxide</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>-</td>
</tr>
</tbody>
</table>

Acute liver failure (ALF)

Definition of acute liver failure

- Evidence of coagulation abnormality (usually an INR $\geq 1.5$) and any degree of mental alteration (encephalopathy) in a patient without preexisting liver disease, and length of illness considered $< 26$ weeks.
- Other definitions (fulminant, subfulminant etc) are not particularly helpful since they do not have prognostic significance distinct from the cause of the illness.

*(ALF Study Group, EASL Conference, Copenhagen, September 2007)*
Artificial and bioartificial support systems for liver failure

Goals in ALF

• **Primary goals**
  ✓ To bridge patients to recovery and normal health

• **Secondary goals**
  ✓ To stop the progression of liver failure
  ✓ To prevent or improve extrahepatic complications
  ✓ To bridge to liver transplantation
  ✓ To improve the outcome of liver transplantation
Artificial and bioartificial support systems for liver failure
Thirty-day survival in patients with FHF and SHF treated with BAL or conventional intensive treatment

<table>
<thead>
<tr>
<th>Etiology</th>
<th>N°</th>
<th>Control Survivors (%)</th>
<th>BAL Survivors (%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients</td>
<td>171</td>
<td>62</td>
<td>71</td>
<td>N.S.</td>
</tr>
<tr>
<td>FHF/SHF</td>
<td>147</td>
<td>59</td>
<td>73</td>
<td>N.S.</td>
</tr>
<tr>
<td>PNF</td>
<td>24</td>
<td>75</td>
<td>58</td>
<td>N.S.</td>
</tr>
</tbody>
</table>

Artificial and bioartificial support systems for liver failure

Thirty-day survival rates in transplanted versus nontransplanted patients

<table>
<thead>
<tr>
<th>Etiology</th>
<th>N°</th>
<th>Control Survivors (%)</th>
<th>BAL Survivors (%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transplanted pts</td>
<td>94</td>
<td>80</td>
<td>89</td>
<td>N.S.</td>
</tr>
<tr>
<td>Nontransplanted pts</td>
<td>77</td>
<td>38</td>
<td>50</td>
<td>N.S.</td>
</tr>
</tbody>
</table>

Time to death in patients with FHF and SHF treated with BAL or conventional intensive treatment

\[ P = \text{N.S.} \]

Artificial and bioartificial support systems for liver failure

Artificial and bioartificial support systems for liver failure

Time to death in patients with FHF and SHF with known etiology

BAL (Hepatassist)

Conventional intensive treatment

P <0.01

Artificial and bioartificial support systems for liver failure

MARS, molecular adsorbents recirculating system.
Artificial and bioartificial support systems for liver failure

MARS for ACLF and ALF: mortality

ACLF
- Mitzner 2001
- Heeman 2002
- TOTAL

ALF
- Schmidt 2003
- El-Banayosy 2003
- TOTAL

P = N.S.

ALF = 30 patients

Favour MARS

Favour control

0.1  0.3  1  2  4

Fulmar Study: Inclusion criteria and Endpoints

**Inclusion criteria**

- Patients with Fulminant (FHF) or subfulminant hepatic failure (SHF)
- Age > 18 - 70 years
- For FHF and SHF not due to paracetamol
  - Clichy or King’s college criteria
- For paracetamol-induced fulminant hepatic failure
  - King’s college criteria
- Informed and written patient or a close relative consent

**End points**

- Primary endpoint: Six months survival
- Coprimary endpoint: Six months Transplant free survival

Artificial and bioartificial support systems for liver failure

Patient account (Aug 2004 - Dec 2007)

110 Patients randomized

CMT n = 53
33 NP - 20 P

Excluded: 4 patients

n = 49
30 NP - 19 P

102 pts ITT


MARS n = 57
35 NP - 22 P

Excluded: 4 patients

n = 53
33 NP - 20 P

7 pts No MARS
7 pts: <4h session

n = 39
23 NP - 16 P

88 pts PP
### Artificial and bioartificial support systems for liver failure

#### Timing to liver transplantation (LT)

**ITT population n= 66/102**

<table>
<thead>
<tr>
<th></th>
<th>CMT n= 49</th>
<th>MARS n= 53</th>
<th>Total n=102</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Timing (hours)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Delay Random/Listing</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (hours)</td>
<td>1.6 ± 7.4</td>
<td>5.4 ± 18.4</td>
<td>3.7 ± 14.6</td>
</tr>
<tr>
<td>Median (hours)</td>
<td>0.8</td>
<td>1.1</td>
<td>1</td>
</tr>
<tr>
<td>Delay Listing/LT (incision)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (hours)</td>
<td>22.9 ± 14.4</td>
<td>18.5 ± 13.4</td>
<td>21.3 ± 13.8</td>
</tr>
<tr>
<td>Median (hours)</td>
<td>20.1</td>
<td>15.4</td>
<td>16.2</td>
</tr>
</tbody>
</table>

- 75% of the patients were transplanted within 24h
- 89.4% of the patients were transplanted within 48h

Artificial and bioartificial support systems for liver failure

Results: 6 month survival patients (ITT analysis)

Artificial and bioartificial support systems for liver failure

Results of CoPrimary endpoint
Transplant free survival / Etiology (ITT analysis)

Non Paracetamol

Paracetamol

Artificial and bioartificial support systems for liver failure

Transplant Free survival by number of therapeutic sessions in patients randomized to MARS

Transplant free survival curve for ITT patients with Mars treatment according to the number of Mars sessions $\geq 3$ or $<3$

- $<3$ sessions $n=39$: 3 survivors w/t LT
- $\geq 3$ sessions $n=14$: 7 survivors w/t LT

Logrank test: $p<0.0001$

Artificial and bioartificial support systems for liver failure

**Definition of acute on chronic liver failure**

- Acute hepatic insult manifesting as jaundice and coagulopathy, complicated within 4 weeks by ascites and/or encephalopathy in a patients with previously diagnosed or undiagnosed liver disease.
- As far as jaundice, total serum bilirubin should be $\geq 5$ mg/dl. Coagulopathy should be indicated by INR $\geq 1.5$ or prothrombin activity $< 40\%$.

*(APASL Study Group, Hepatol. Int. 2009 ; 3 :269-282.)*
Artificial and bioartificial support systems for liver failure

Goals in ACLF

• **Primary goals**
  ✓ To bridge patients to the state before decompensation

• **Secondary goals**
  ✓ To stop the progression of liver failure
  ✓ To prevent or improve extrahepatic complications
  ✓ To bridge to liver transplantation
  ✓ To improve the outcome of liver transplantation
Artificial and bioartificial support systems for liver failure

MARS, molecular adsorbents recirculating system.
Artificial and bioartificial support systems for liver failure

MARS for ACLF and ALF: mortality

ACLF
- Mitzner 2001
- Heeman 2002
- TOTAL

P = N.S.

ACLF = 37 patients

ALF
- Schmidt 2003
- El-Banayosy 2003
- TOTAL

P = N.S.

Favour MARS

Favour control

Relief Study: Inclusion and exclusion criteria and Endpoint

**Inclusion criteria**

- Acutely decompensated liver cirrhosis
- Bilirubin > 5 mg/dl (without evidence of extrahepatic origin)
  and at least one of:
  - HRS (International Ascites Club) and/or
  - Hepatic encephalopathy ≥ II and/or
  - Progressive hyperbilirubinemia (Bilirubin > 20 mg/dl)

**Exclusion criteria**

- Platelet count less than 50000/mm³
- INR >2.3 or DIC
- Need for renal replacement or intrinsic renal disease
- Uncontrolled infection

**End point**: 28 day survival

*R. Banares et al. J. Hepatol. 2010 ; 52 : S459 (Abstract).*
Artificial and bioartificial support systems for liver failure

Relief Study: study flow chart (1)

Screened patients for the trial = 397

Patients eligible n = 189

SMT

Day 0 N=189

Day 4

Day 7

Day 14

Day 21

Day 28

Patients not eligible for the trial = 208

Main reasons for no inclusion
No inclusion criteria n=68
INR>2.3 n=43
Platelet count< 50000/mm³ n=34
No consent n=23

Mean (SD) number of sessions:
6.5 (3.1) sessions/patient

Duration of MARS sessions: 6-8 h

Randomized patients
n=189

SMT
n=95

Low platelets count (2)
No inclusion criteria (2)
Advanced cancer (1)

SMT
n=89

Inclusion criteria violations

Intention-to-treat population  n = 179

MARS
n=95

Low platelets count (3)
No inclusion criteria (1)
Bleeding just before inclusion (1)

MARS
n=90

Early liver transplantation (3)
Death day 1 before SMT (1)

SMT
n=85

Per Protocol Population n=156

MARS
n=71

Early liver transplantation (2)
Withdrawal of consent (5)
Less than 3 MARS sessions (12)

<table>
<thead>
<tr>
<th>Variable</th>
<th>SMT (n=85)</th>
<th>SMT+ MARS (n=71)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>50 (11)</td>
<td>51.8 (10.4)</td>
<td>NS</td>
</tr>
<tr>
<td>Sex (male (%))</td>
<td>61 (71.8 %)</td>
<td>46 (64.8 %)</td>
<td>NS</td>
</tr>
<tr>
<td>Etiology of liver disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcohol</td>
<td>80 (94.1 %)</td>
<td>64 (90.1 %)</td>
<td>NS</td>
</tr>
<tr>
<td>Viral hepatitis</td>
<td>7 (8.2 %)</td>
<td>5 (7 %)</td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td>6 (7.1 %)</td>
<td>9 (12.6 %)</td>
<td></td>
</tr>
<tr>
<td>Alcohol abuse (n (%))</td>
<td>66 (77.6 %)</td>
<td>55 (77.5 %)</td>
<td>NS</td>
</tr>
<tr>
<td>Infection (n (%))</td>
<td>26 (30.6 %)</td>
<td>20 (28.2 %)</td>
<td>NS</td>
</tr>
<tr>
<td>GI Bleeding (n (%))</td>
<td>12 (14.1 %)</td>
<td>8 (11.3 %)</td>
<td>NS</td>
</tr>
<tr>
<td>Dehydration (n (%))</td>
<td>8 (9.4 %)</td>
<td>6 (8.5 %)</td>
<td>NS</td>
</tr>
<tr>
<td>SBP (n (%))</td>
<td>6 (7.1 %)</td>
<td>12 (16.9 %)</td>
<td>NS</td>
</tr>
<tr>
<td>Others (n (%))</td>
<td>5 (5.9 %)</td>
<td>1 (1.4 %)</td>
<td>NS</td>
</tr>
<tr>
<td>More than one precipitating event n (%)</td>
<td>32 (37.6 %)</td>
<td>29 (40.8 %)</td>
<td>NS</td>
</tr>
<tr>
<td>Number of precipitating events (median (range)</td>
<td>1 (1-4)</td>
<td>1 (1-3)</td>
<td>NS</td>
</tr>
</tbody>
</table>

### Artificial and bioartificial support systems for liver failure

#### Relief Study: features of “Per Protocol” population (2)

<table>
<thead>
<tr>
<th>Variable</th>
<th>SMT (n=85)</th>
<th>SMT+MARS (n=71)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Progressive hyperbilirubinemia n° (%)</td>
<td>60 (70.6 %)</td>
<td>46 (64.8 %)</td>
<td>NS</td>
</tr>
<tr>
<td>HRS n° (%)</td>
<td>45 (52.9 %)</td>
<td>37 (52.1 %)</td>
<td>NS</td>
</tr>
<tr>
<td>Encephalopathy ≥ grade II n° (%)</td>
<td>37 (43.5 %)</td>
<td>28 (39.4 %)</td>
<td>NS</td>
</tr>
<tr>
<td>Bilirubin (mg/dl)</td>
<td>27.0 (12.3)</td>
<td>26.8 (11.8)</td>
<td>NS</td>
</tr>
<tr>
<td>Albumin (g/L)</td>
<td>28.1 (9.9)</td>
<td>27.3 (6.3)</td>
<td>NS</td>
</tr>
<tr>
<td>Serum creatinine</td>
<td>2.27 (2.07)</td>
<td>2.50 (2.20)</td>
<td>NS</td>
</tr>
<tr>
<td>INR</td>
<td>1.78 (0.33)</td>
<td>1.74 (0.31)</td>
<td>NS</td>
</tr>
<tr>
<td>Hematocrit</td>
<td>29.3 (6.0)</td>
<td>28.4 (4.8)</td>
<td>NS</td>
</tr>
<tr>
<td>Leucocytes</td>
<td>15.6 (11.0)</td>
<td>16 (9.6)</td>
<td>NS</td>
</tr>
<tr>
<td>Platelet count</td>
<td>120.3 (72.3)</td>
<td>130.9 (75.2)</td>
<td>NS</td>
</tr>
<tr>
<td>MELD &gt; 20 n° (%)</td>
<td>59 (69.4 %)</td>
<td>58 (81.7 %)</td>
<td>NS</td>
</tr>
</tbody>
</table>

*R. Banares et al. J. Hepatol. 2010 ; 52 : S459 (Abstract).*
Artificial and bioartificial support systems for liver failure

Relief Study: 28-day transplant free survival

ITT population

Per Protocol population

\[ P = \text{N.S.} \]

\[ P = \text{N.S.} \]

Artificial and bioartificial support systems for liver failure
Artificial and bioartificial support systems for liver failure

Reduction of plasma bilirubin levels by MARS vs. Prometheus

Mean arterial pressure before and after extracorporeal albumin dialysis (MARS or PROMETHEUS)

<table>
<thead>
<tr>
<th>PARAMETER</th>
<th>MARS</th>
<th>PROMETHEUS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before treatment</td>
<td>After treatment</td>
</tr>
<tr>
<td>Heart rate (bpm)</td>
<td>77 ± 7</td>
<td>83 ± 6</td>
</tr>
<tr>
<td>Mean arterial pressure (mm Hg)</td>
<td>67 ± 4</td>
<td>76 ± 3*</td>
</tr>
<tr>
<td>Stroke volume (ml)</td>
<td>107 ± 18</td>
<td>120 ± 15*</td>
</tr>
<tr>
<td>Systemic vascular resistance</td>
<td>1088 ± 88</td>
<td>1219 ± 93</td>
</tr>
</tbody>
</table>

* p < 0.05 vs before
# p < 0.001 vs before

Helios Study: Aim, inclusion criteria and Endpoint

✓ **Aim:** Evaluation of benefit of Prometheus therapy in patients with acute decompensation of chronic liver disease

✓ **Inclusion criteria:** CTP score >10 and bilirubin > 5mg/dl

✓ **Primary endpoint:** Survival at 28 days and 3 months

*K. Rifai et al. J. Hepatol. 2010; 52: S3 (Abstract).*
Artificial and bioartificial support systems for liver failure

Helios Study: 28-day transplant free survival

Day 28
SMT+FPSA: 66%
SMT: 63%
Diff. ~ 3%, NS

Day 90
SMT+FPSA: 47%
SMT: 38%
Diff. ~ 9%, NS

Artificial and bioartificial support systems for liver failure

Helios Study: 28-day transplant free survival in subgroup of patients with MELD > 30

Artificial and bioartificial support systems for liver failure

Helios Study: 28-day transplant free survival in subgroup of patients with type 1 HRS

Day 90
Diff. ~ 36%; p<0.05

Day 28
Diff. ~ 23%; NS

Artificial and bioartificial support systems for liver failure

Probability of survival in patients with HRS treated with extracorporeal albumin dialysis (MARS)

Artificial and bioartificial support systems for liver failure

Mean improvement of grade 3 or 4 hepatic encephalopathy in patients with cirrhosis according to treatment: MARS vs standard medical treatment (STM)

P < 0.05

Artificial and bioartificial support systems for liver failure

Intensity of pruritus assessed by visual analogue score (VAS) before and after treatment with MARS

Artificial and bioartificial support systems for liver failure

Comment (1)

The question “Is there life in MARS? still remains open”
Artificial and bioartificial support systems for liver failure

Comment (2)

“Promethues still remains a mith”
Artificial and bioartificial support systems for liver failure

What can be specifically stated?

Do artificial support system recover in a definitive way hepatic function in ALF or ACLF so to increase long or mid-term free transplant survival?

No evidence

Do artificial support systems improve the bridging to liver transplantation in patients with ALF or ACLF?

Only in subgroups

Do artificial support system improve outcome of liver transplantation in patients with ALF or ACLF?

No evidence
Mortality in patients with acute liver failure or acute on chronic liver failure remains unacceptably high. To the day, in spite of some beneficial effects in subgroups of patients with ALF and ACLF the artificial and bioartificial liver systems have failed to live up their initial promise and currently cannot be recommended for the treatment of patients outside of carefully controlled clinical trials.
Potential detrimental substances in ALF and ACLF

• **Water soluble free substances**
  ✓ Creatinine
  ✓ Urea

• **Albumin-bound substances**
  ✓ bilirubin
  ✓ bile acids
  ✓ ammonia
  ✓ mercaptans
  ✓ false neurotranmitters
  ✓ tryptophan
  ✓ cytokines
  ✓ nitric oxide
  ✓ prostacyclin
  ✓ others
Characteristics of the liver

- 1.5 kg in average adult
- Blood throughput 1450 ml/min
  - Highly vascularized
  - High oxygen demand
- 5 cell types present
- Many varied functions performed
  - Maintenance of homeostasis
  - Glucose uptake/release
  - Ammonia clearance through urea production
  - Lipid processing
  - Plasma protein synthesis
  - Bile formation
  - Xenobiotic metabolism
Artificial and bioartificial support systems for liver failure

The “cytokine storm” in ACLF

Artificial and bioartificial support systems for liver failure

**TNFα and IL-10 production by peripheral monocyte after stimulation with LPS in study groups**

<table>
<thead>
<tr>
<th>Cytokine</th>
<th>ACLF (early)</th>
<th>ACLF (late)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>TNFα (pg/ml)</td>
<td>2305.4 ± 732.7</td>
<td>1173.1 ± 513.9</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>IL-10 (pg/ml)</td>
<td>53.9 ± 19.8</td>
<td>78.3 ± 27.4</td>
<td>&lt; 0.01</td>
</tr>
</tbody>
</table>

Artificial and bioartificial support systems for liver failure

Interaction between the pro-inflammatory (SIRS) and anti-inflammatory (CARS) in the evolution of sepsis

### Artificial and bioartificial support systems for liver failure

#### Effects of MARS and Prometheus on plasma cytokines

<table>
<thead>
<tr>
<th>Molecular Weight (KDa)</th>
<th>Plasma clearance (ml/min)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MARS</td>
<td>Prometheus</td>
</tr>
<tr>
<td>IL-6 21-29</td>
<td>3 (1-6)</td>
<td>4 (2-20)</td>
</tr>
<tr>
<td>IL-8 8-10</td>
<td>17 (0-28)</td>
<td>3 (1-35)</td>
</tr>
<tr>
<td>IL-10 35-40</td>
<td>16 (5-25)*</td>
<td>46 (19-60)</td>
</tr>
<tr>
<td>TNFα 29</td>
<td>2 (2-9)</td>
<td>12 (3-16)</td>
</tr>
</tbody>
</table>

*P <0.05 vs IL-6

*V. Stadlbauer et al. Crit. Care 2006 ; 10 : (on line).*
Cytokins and hepatocyte death

Drugs
Bacterial infections and/or endotoxins
Viral infections

Kupffer cells

Release of cytokines (TNFα)

Recruitment of liver PMN

Recruitment of T cells

Release of cytokines (TNFα)

Hepatocyte death

ROS

Artificial and bioartificial support systems for liver failure

Signal transduction pathways during the priming phase of liver regeneration: interactions between Kupffer cells and hepatocytes

Y. Iimuro et al.  Gastroenterol. Res. Pract. 2010 ; (on line)
Artificial and bioartificial support systems for liver failure
Artificial and bioartificial support systems for liver failure

Effect of tenofovir on survival in patients with spontaneous reactivation of Hepatitis B presenting as acute-on-chronic liver failure

Artificial and bioartificial support systems for liver failure

Transplant free survival in patients with non parecetamol-induced ALF treated with N-acetylcysteine (NAC) or standard medical therapy (STM)

P < 0.05

WM. Lee et al. Gastroenterology 2009; 137: 856-864.
Artificial and bioartificial support systems for liver failure

Implications for research

- Further studies are needed to better clarify the pathophysiology of ALF and ACLF and, as a consequence to evaluate the impact of artificial and bioartificial systems on it.
- Randomised trails on artificial and bioartificial support systems versus standard therapy are warranted.
- Hepatologists ought to designe randomised trials allocating patients to one support system plus “standard medical therapy” versus “standard medical therapy”.
- Hepatologists ought to be aware that “standard medical therapy” is rapidly changing in this field.