HIV and HBV/HCV coinfection and liver transplantation:

Results

Jean-Charles Duclos-Vallée

CENTRE HEPATO-BILIAIRE
HÔPITAL PAUL BROUSSE
VILLEJUIF
HIV Coinfection Shortens the Survival of Patients with HCV Decompensated Cirrhosis

Median survival = 16 months

<table>
<thead>
<tr>
<th>Survival</th>
<th>1-year</th>
<th>2-year</th>
<th>5-year</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV+</td>
<td>54%</td>
<td>40%</td>
<td>25%</td>
</tr>
<tr>
<td>HIV-</td>
<td>74%</td>
<td>61%</td>
<td>44%</td>
</tr>
</tbody>
</table>

Probability of patient survival according to HIV serostatus

Pineda et al. Hepatology 2005
Liver Transplantation in Adults Coinfected with HIV under HAART

**Preliminary Experience**

*Prachalias et al. Transplantation 2001*

<table>
<thead>
<tr>
<th>Patients</th>
<th>Diagnosis</th>
<th>Outcome Post LT</th>
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<tbody>
<tr>
<td>1</td>
<td>HCV</td>
<td>Died (25 months)</td>
</tr>
<tr>
<td>2</td>
<td>HCV</td>
<td>Died (15 months)</td>
</tr>
<tr>
<td>3</td>
<td>HCV</td>
<td>Died (6 months)</td>
</tr>
<tr>
<td>4</td>
<td>HBV</td>
<td>Alive (24 months)</td>
</tr>
<tr>
<td>5</td>
<td>NANB</td>
<td>Alive (4 months)</td>
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</table>
## LIVER TRANSPLANTATION IN HIV-HCV PATIENTS
### Pittsburgh and Miami (1997-2001)

<table>
<thead>
<tr>
<th>Patient</th>
<th>OLT date</th>
<th>Outcome</th>
<th>Cause</th>
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<tr>
<td>6</td>
<td>May 2001</td>
<td>Alive</td>
<td></td>
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<tr>
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<td>Alive</td>
<td></td>
</tr>
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<td>8</td>
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<td>Alive</td>
<td></td>
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<tr>
<td>9</td>
<td>Jan 1999</td>
<td>Died (12 days)</td>
<td>Acute CR</td>
</tr>
<tr>
<td>10</td>
<td>Mar 1999</td>
<td>Died (570 days)</td>
<td>CR/HCV</td>
</tr>
<tr>
<td>12</td>
<td>Oct 2000</td>
<td>Alive</td>
<td></td>
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<td>Alive</td>
<td></td>
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<tr>
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<td>Oct 2001</td>
<td>Alive</td>
<td></td>
</tr>
<tr>
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<td>Nov 2001</td>
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_Neff et al. Liver Transpl 2003_
## LIVER TRANSPLANTATION IN HIV-HBV PATIENTS

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*Neff et al. Liver Transpl 2003*
**PRETRANSPLANT INCLUSION AND EXCLUSION CRITERIA**

**Inclusion:**
- HIV viral load -
- Limited or no opportunistic complications
- CD4+ > 250/mL for the past 6 months
- History of compliance with medical protocol

**Exclusion:**
- Ongoing opportunistic infection or cancer
- History of any neoplasm except hepatocellular carcinoma
Paul Brousse Experience
November 2000 - October 2005

$n = 41$ patients transplanted

- HCV Cirrhosis
  - $n=34$
  - (HCC: $n=3$

- HBV Cirrhosis
  - $n=6$
  - (Delta coinfection: $n=2$
  - (HCC: $n=1$

- Fulminant Hepatitis: $n=1$
8 patients died

HCV recurrence and mitochondrial toxicity: n=5
Acute pancreatitis: n=1
Pancreatic adenocarcinoma: n=1
Cerebral hemorrhage: n=1
HCV viral recurrence

HCV viral load

Viral load at 6 months

- Co-infected: 6.8 ± 0.4
- Monoinfected: 6.0 ± 1

P = 0.03
HCV viral recurrence
Severity of fibrosis
January 1999 - June 2004

n= 23 HIV/HCV +

Rate of Fibrosis between M12 and M16
= Time from LT/Metavir F

Fibrosing cholestasis
Hepatitis n=1
M24
Post LT

Coinfected (n=23): 1.5 ± 1.4
P=0.03

Monoinfected (n=44): 0.8 ± 0.5
### HCV viral recurrence

**Effect of Antiviral Therapy**

<table>
<thead>
<tr>
<th></th>
<th>Co-infected patients</th>
<th>Monoinfected patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pegylated interferon a 2-b + ribavirin</td>
<td>13/22 (59 %)</td>
<td>14/44 (32 %)</td>
</tr>
<tr>
<td>Virological response</td>
<td>3/13 (23%)</td>
<td>10/14 (71%)</td>
</tr>
</tbody>
</table>
Secondary effect of anti-HCV therapy

Anti HCV therapy was stopped in 5 patients

- Pancreatitis : n = 1
- Lethal lactic acidosis : n = 1
- Intense Asthenia : n = 3

13/22 (59%) treated
Mitochondrial toxicity

*Microvesicular steatosis*

Microvesicular steatosis

*range (10%-50\%) observed in 8/19 (42\%) patients*
## Mitochondrial toxicity

**Comparison of Liver mtDNA in HIV+/HCV+ Patients and HIV Negative Controls**

<table>
<thead>
<tr>
<th>Patients</th>
<th>Liver mt DNA (copies number/ng total DNA)</th>
<th>IV complex Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV+/HCV+ (n=5)</td>
<td>26,511 (5817-143010)</td>
<td>0&lt;&lt;4 nmol/min/mg</td>
</tr>
<tr>
<td>HIV-/HCV+ (1 year post LT) (n=8)</td>
<td>19,523 (203207-611111) ( p=0.01 )</td>
<td>In 6/7 patients studied</td>
</tr>
</tbody>
</table>

*Duclos-Vallee J Hepatol 2005*
CD4 Count and HIV viral load
During the Post-LT Course
n=7
Bacterial and opportunistic infections

<table>
<thead>
<tr>
<th>Bacterial infection</th>
<th>Opportunistic infections</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Monoinfected Patients</strong></td>
<td><strong>Coinfected Patients</strong></td>
</tr>
<tr>
<td>16/44 (36%)</td>
<td>3/23 (13%)</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\[ p=0.03 \]
Drug Interaction
In HIV Liver Transplant Patients

Teicher et al. Submitted

+ LPV/RTV
⇒ Tacrolimus
0.5mg / 10 or 15 days
Survival analysis

2-year survival:
- HIV+/HCV (n=23): 72%
- HIV-/HCV (n=44): 92%

Log rank p=0.07
Survival of Transplanted Monoinfected HCV (4062 Unos) and Coinfected HCV-HIV (15)

Proportion surviving

Months since OLTX

HCV+/HIV-/OLTX

HCV+/HIV+/OLTX

p = 0.06

Ragni M et al, J Infect Dis, 2003;188:1412–20
Liver Transplantation In HIV-HBV Patients  
$n=5$

<table>
<thead>
<tr>
<th>Patients</th>
<th>Post LT HBV therapy</th>
<th>Follow-up</th>
<th>Clinical status</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALE.</td>
<td>HB1g+Lam+Tenof.</td>
<td>M36</td>
<td>Well</td>
</tr>
<tr>
<td>MAH.</td>
<td>HB1g+Lam+Tenof.</td>
<td>M31</td>
<td>Well</td>
</tr>
<tr>
<td>BON.</td>
<td>HB1g+Lam+Tenof.</td>
<td>M24</td>
<td>Well</td>
</tr>
<tr>
<td>MONG.</td>
<td>HB1g+Lam+Tenof.</td>
<td>M12</td>
<td>Well</td>
</tr>
<tr>
<td>GREY.</td>
<td>HB1g+Lam+Tenof.</td>
<td>M12</td>
<td>Well</td>
</tr>
</tbody>
</table>
Conclusions

• Feasible
• **HBV-HIV:** Excellent
• **HCV-HIV:** Difficult
  – Mitochondrial toxicity
    » Avoid DDI, D4T, AZT
    » Change HAART if microvesicular steatosis
  – HCV recurrence
    » Early Antiviral therapy
A Multidisciplinary Approach

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T Antonini
M Gigou
C Danet
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C Tanguy
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AM Roque-Afonso
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E Dussaix

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M Sebagh
MP Bralet
C Guettier