Liver transplant & HIV
Debate: the cons
This is about risk and utility

Disclosures: ‘I’m a why not person’  
Janssen/ MSD/ Gilead/ BMS/ GSK  
Novartis/ Roche/ Abbott/ Astellas

This is a two-sided conversation…

I will be deliberatively controversial

Institutional risk: allocation/ outcomes

benefit vs need vs equity
‘what does the greatest good?’  
The losers in LT have no voice…
Peter is a master, proponent and has a vast experience but I will ‘battle complacency, advance commitment…’ cf IAPAC

HIV and LT
Does this fulfill 50% 5 year survival
The patient as a package

ALF
Too late/ too ad hoc

Non HCV/HIV
Reasonable data but referred late
Timing

HCV/HIV
Poor outcomes
LD- a complex individual

45 year old female - Italian - film/media lecturer

HCV diagnosed 1992 brief IVDU G1 [brother, parents HCV, partner died HIV] HIV CD4 660 HIV 4,000 copies no cART

Cirrhotic AFP 274 fluctuating - No formal hepatology input till...

Referred 1/08 - decompensation ascites/ SBP on return Italy MELD 16 [INR 2.14/ BR 5.0g/dl/ Creat 64]

Kings 3/08 MELD 24 UKELD 68 [INR 2.2/ BR 9.8g/dl/ Creat 86/ Alb 19]

Listed with priority cART - Truvada (3TC/tenofovir/ raltegavir)

Ambivalence, ‘can I wait?’ episode of encephalopathy requiring ICU Psychosocial issues / NOK becomes more apparent
LD- a complex individual

MELD 26 UKELD 73
LT DD graft It 13 hrs significant fluid shift  DR CMV +/+ 

Initial graft function good
Respiratory issues slow wean   ward 9 days

D5 Increasing cholestasis  BR 6 AST 530 TAC

DILI/ AR/ HCV/ CMV?
CMV - $10^5$ - valganciclovir
HCV 1.6 x $10^7$
cART stopped
Progressive ↑BR

Chest- aspergillosis/ effusion/ hydropneumothorax
VRE- Klebsiella - vanc/ meropenem/amikacin
Multi organ failure/ HITS
Died day 38
Liver Transplantation
Number of deceased donors and transplants in the UK, 1 April 2000 - 31 March 2010, and patients on the active transplant lists at 31 March.

Deceased donors, transplants and transplant waiting list

LIVERS

Number

- Donors
- Transplants
- Transplant list

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<td>LIVERS</td>
<td>175</td>
<td>190</td>
<td>264</td>
<td>365</td>
<td>314</td>
<td>268</td>
<td>338</td>
<td>374</td>
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<td>559</td>
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<tbody>
<tr>
<td>Number</td>
<td>688 705</td>
<td>668 686</td>
<td>637 649</td>
<td>611 600</td>
<td>636 647</td>
<td>632 633</td>
<td>676 657</td>
<td>706 679</td>
<td>712 675</td>
<td>783 741</td>
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Donor Rates
Where are we now?

Deceased organ donor rates for Europe and the USA, 2010

<table>
<thead>
<tr>
<th>Country</th>
<th>Donors pmp</th>
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<tbody>
<tr>
<td>Spain</td>
<td>32.0</td>
</tr>
<tr>
<td>Croatia</td>
<td>30.7</td>
</tr>
<tr>
<td>Portugal</td>
<td>30.2</td>
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<tr>
<td>USA</td>
<td>25.0</td>
</tr>
<tr>
<td>France</td>
<td>23.8</td>
</tr>
<tr>
<td>Italy</td>
<td>21.6</td>
</tr>
<tr>
<td>Norway</td>
<td>20.8</td>
</tr>
<tr>
<td>Finland</td>
<td>17.0</td>
</tr>
<tr>
<td>Slovakia</td>
<td>16.8</td>
</tr>
<tr>
<td>UK</td>
<td>16.4</td>
</tr>
<tr>
<td>Hungary</td>
<td>15.9</td>
</tr>
<tr>
<td>Germany</td>
<td>15.8</td>
</tr>
<tr>
<td>Latvia</td>
<td>14.8</td>
</tr>
<tr>
<td>The Netherlands</td>
<td>13.7</td>
</tr>
<tr>
<td>Poland</td>
<td>13.3</td>
</tr>
<tr>
<td>Denmark</td>
<td>13.0</td>
</tr>
<tr>
<td>Sweden</td>
<td>12.6</td>
</tr>
<tr>
<td>Switzerland</td>
<td>12.6</td>
</tr>
<tr>
<td>Greece</td>
<td>3.9</td>
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Increase in number of deceased donors

<table>
<thead>
<tr>
<th>Year</th>
<th>DBD</th>
<th>DCD</th>
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<tbody>
<tr>
<td>2002-03</td>
<td>716</td>
<td>61</td>
</tr>
<tr>
<td>2003-04</td>
<td>697</td>
<td>73</td>
</tr>
<tr>
<td>2004-05</td>
<td>664</td>
<td>87</td>
</tr>
<tr>
<td>2005-06</td>
<td>637</td>
<td>127</td>
</tr>
<tr>
<td>2006-07</td>
<td>634</td>
<td>159</td>
</tr>
<tr>
<td>2007-08</td>
<td>609</td>
<td>200</td>
</tr>
<tr>
<td>2008-09</td>
<td>611</td>
<td>288</td>
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<tr>
<td>2009-10</td>
<td>624</td>
<td>335</td>
</tr>
<tr>
<td>2010-11</td>
<td>637</td>
<td>373</td>
</tr>
<tr>
<td>2011-12</td>
<td>652</td>
<td>436</td>
</tr>
</tbody>
</table>
Current state

‘few people have the imagination for reality…’

Johann Wolfgang von Goethe (1749-1832)
THE SILENT PANDEMIC
TACKLING HEPATITIS C WITH POLICY INNOVATION
A report from the Economist Intelligence Unit.
Projected Prevalence of Chronic HCV, Cirrhosis, and Complications

Projected Number of Patients With Decompensated Cirrhosis and Hepatocellular Carcinoma

Number of Cases

Year


Hepatocellular Carcinoma (HCC)

Decompensated Cirrhosis

# Overcoming Barriers to Care for Hepatitis C


<table>
<thead>
<tr>
<th>Year</th>
<th>Deaths to which Hepatitis C Contributed</th>
<th>Transplantation for HCV-Related Primary Indication (Excluding Hepatoma)</th>
<th>Transplantation for HCV-Related and HBV- or HCV-Related HCC</th>
<th>Patients Treated with Antiviral Therapy for Hepatitis C in U.S. (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>no. of patients</td>
<td>number</td>
<td>number</td>
<td>number</td>
</tr>
<tr>
<td>2002</td>
<td>4839</td>
<td>1904</td>
<td>752</td>
<td>126,040 (125,449–126,649)</td>
</tr>
<tr>
<td>2003</td>
<td>4616</td>
<td>1862</td>
<td>829</td>
<td>144,276 (143,616–144,943)</td>
</tr>
<tr>
<td>2004</td>
<td>4586</td>
<td>2022</td>
<td>889</td>
<td>107,131 (106,653–107,614)</td>
</tr>
<tr>
<td>2005</td>
<td>4767</td>
<td>2040</td>
<td>988</td>
<td>114,197 (113,580–114,823)</td>
</tr>
<tr>
<td>2006</td>
<td>6415</td>
<td>1942</td>
<td>1149</td>
<td>88,083 (87,685–88,486)</td>
</tr>
<tr>
<td>2007</td>
<td>6572</td>
<td>1799</td>
<td>1247</td>
<td>83,270 (82,897–83,647)</td>
</tr>
</tbody>
</table>

* Data in the column on mortality are from the Centers for Disease Control and Prevention, National Center for Health Statistics, Multiple Cause of Death 1999–2009 (http://wonder.cdc.gov/mcd-icd10.html), and are based on hepatitis C infection (ICD-10, 17.1 and 18.2) declared as a contributing cause on the death certificate; data in the columns on transplantation are from the Organ Procurement and Transplantation Network (as of May 2012); and data in the column on antiretroviral therapy are from Volk et al. CI denotes confidence interval, HBV hepatitis B virus, HCC hepatocellular carcinoma, and HCV hepatitis C virus.
Why do we bother to transplant HCV…?

‘LT should be viewed as a lifelong commitment by both patient & physician’

Liu L, Schiano TD. Clinics in Liver Disease 2007

Should HCV get defined ‘better’ organs?? Transplantation is not an extension of Rx? Hep C u later….? (Ed Gane)
How do we consider consistency of approach, equity of access, justice…’ level playing field’

We all bring our personal prejudices, cultural expectations, value perspectives to the transplant listing meeting…

‘how did he get his disease’

Don’t we?
HIV coinfection Shortens the Survival of Patients with HCV-related Decompensated Cirrhosis
Should we allocate priorities to HIV?

Survival among HCV-infected individuals with and without HIV coinfection

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

No. at risk

HIV-positive 180 75 46 30 19 11 5 3

ESLD/HCC – ‘the agenda is full’ (cf Puoti 2013)

1995-2001: 5x increase in French Mortavic study
(Rosenthal AIDS 2003)

2004 GICAT study 41 cases vs 384 HIV -ve controls younger, sicker, poor survival, little Rx offered
however 15/41 within Milan criteria!
(Puoti AIDS 2004)

2008 US/ Canadian study (Brau N J Hepatol 2008)
63 HIV/HCV vs 266 HCV
26 vs 36 yrs / younger/ similar Rx

2013 Ioannaou Hepatology 2013
24000pts : HCV (18% received Rx), HBV, Diabetes, Alcohol, CD4
are you surprised?
KINGS: LT for HIV: analysis of outcomes suggest HIV/HCV coinfected patients have ‘prohibitively’ poor survival at 5 years

Survival rates at 1 and 5 years: HIV+/HCV group = 64%  
1/95 -5/08  
1% of total activity  
Younger  
Sicker (MELD)  
3 died HCV recurrence/ 2 sepsis

Joshi et al AASLD 2008 Abst6
Survival of HIV-HCV vs HCV mono
More aggressive fibrosis

Log rank $p=0.004$

Time post liver transplantation (months)

Survival

HIV-/HCV+ 81%

HIV+/HCV+ 51%

HIV-/HCV+ 73%

HIV+/HCV+ 91%

The number of patients in each group is indicated

HIV-/HCV+ 44 43 43 40 38 34 25
HIV+/HCV+ 35 33 33 19 12 5 4

Its actually not just about the HIV

Fig. 1. Factors linked to HCV graft fibrosis and to graft loss in HIV/HCV-coinfected transplant recipients.
Epidemiology and Outcome of Infections in Human Immunodeficiency Virus/Hepatitis C Virus–Coinfected Liver Transplant Recipients: A FIPSE/GESIDA Prospective Cohort Study

Asunción Moreno,1 Carlos Cervera,1 Jesús Fortún,2 Marino Blanes,3 Estibalitz Montejo,4 Manuel Abradelo,5 Oscar Len,6 Antonio Rafecas,7 Pilar Martín-Davila,2 Julián Torre-Cisneros,8 Magdalena Salcedo,9 Elisa Cordero,10 Ricardo Lozano,11 Iñaki Pérez,1 Antonio Rimola,1.12 José M. Miró,1 and the OLT-HIV FIPSE Cohort Investigators

84 pts 17 sites 43%mortality at 36 mnths
Severe infection 3x mortality
MELD >15/ AIDS/ non Tac

Liver Trans 2012
Outcomes of Liver Transplant Recipients with Hepatitis C and Human Immunodeficiency Virus Coinfection

Norah A. Terrault,1 Michelle E. Roland,1 Thomas Schiano,2 Lorna Dove,3 Michael T. Wong,4 Fred Poordad,5 Margaret V. Ragni,6 Burc Barin,7 David Simon,8 Kim M. Oltosoff,9 Lynt Johnson,10 Valentina Stosor,11 Dushyantha Jayaweera,12 John Fung,13 Kenneth E. Sherman,14 Aruna Subramaniam,15 J. Michael Millis,16 Douglas Slakey,17 Carl L. Berg,18 Laurie Carlson,1 Linda Ferrell,1 Donald M. Stablein,7 Jonah Odim,19 Lawrence Fox,19 and Peter G. Stock1 for the Solid Organ Transplantation in HIV: Multi-Site Study Investigators

79vs 53% 3 yr survival p<0.001
Do. Or do not. There is no try

HIV-coinfected recipients versus HCV-infected recipients. Our results indicate that HCV per se is not a contraindication to LT in HIV patients, but recipient and donor selection and the management of acute rejection strongly influence outcomes.

Multi centre: proponents Terrault N
Post hoc analysis
IS choice

BMI multi-organ failure
LKD sepsis not HIV
HCV Ab+ve

There is a clear need to acknowledge that a 3-year graft survival rate of 53% both disappoints and fails to provide the basis for a sustainable practice.

JO Grady editorial
‘I have to nothing to but blood, toil, tears and sweat...’

Only few centres offer this...why?
Utility vs innovation and ‘envelope pushing’ is not the norm

Societal debate / education – donation/transplant/HIV?
Have we optimised the basics?
All HIV/liver patients should be on liver friendly regimens (truvada/ raltegavir)?
Vaccinate? HCC screening?
Higher stringency for lifestyle issues
Alcohol?
Nominated centres/ resource?
Specific scoring system – ‘prioritization’ is a dangerous word?
Every patient coming to transplant needs a trial of HCV antiviral therapy?
Final thought

Reality is merely an illusion, Albeit a very persistent one …

Albert Einstein 1879-1955
Kings Liver Course May 17th:
Hepatitis Masterclass: at the cutting edge