Use of HIV(+) or HCV(+) grafts

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Disclosures

Speaker bureau for Abbvie, Bayer, Bristol-Myers Squibb, Gilead Sciences, Janssen Pharmaceuticals, MSD and Novartis
AGENDA

1. HCV(+) graft Epidemiology

2. HCV + Recipients with either HCV(+) OR HCV(-) grafts:
   a. Head-to-head comparison
   b. Role of genotype
   c. Role of Age
   d. Role of graft Fibrosis

3. HCV(+) DONORS in HCV(−) recipients
Dealing with organ shortage

Despite concerted efforts to safely expand the donor organ pool, there is a widening gap between organ availability and demand.

Activity of liver transplantation in France

+80%

+40%
Anti-HCV+ liver grafts represent an important resource

- Worldwide, an estimated 70-130 million people have HCV infection\(^1\)
- Prevalence of HCV differs dramatically between regions\(^1\)

### HCV+ graft utilization

Estimated Risk of Human Immunodeficiency Virus and Hepatitis C Virus Infection among Potential Organ Donors from 17 Organ Procurement Organizations in the United States

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Risk status¹</th>
<th>N</th>
<th>Prevalence (%) for organ donors in study²</th>
<th>Prevalence (%) blood donors ³</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCV</td>
<td>Normal risk</td>
<td>10997</td>
<td>3.45</td>
<td>0.17</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(3.10–3.85)</td>
<td>(0.16–0.18)</td>
</tr>
<tr>
<td></td>
<td>High risk</td>
<td>1169</td>
<td>18.20</td>
<td>0.17</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(15.74–20.91)</td>
<td>(0.16–0.18)</td>
</tr>
<tr>
<td></td>
<td>Missing risk</td>
<td>1183</td>
<td>12.88</td>
<td>0.17</td>
</tr>
<tr>
<td></td>
<td>status</td>
<td></td>
<td>(10.83–15.08)</td>
<td>(0.16–0.18)</td>
</tr>
<tr>
<td></td>
<td>All potential donors</td>
<td>13349</td>
<td>5.58</td>
<td>0.17</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(5.15–6.06)</td>
<td>(0.16–0.18)</td>
</tr>
</tbody>
</table>

Ellingsona K et al. AJT 2011; 11: 1201–1208
HCV+ graft utilization

LONG-TERM OUTCOMES IN LIVER TRANSPLANT RECIPIENTS TRANSPLANTED FROM HCV-POSITIVE DONORS
Maria Stepanova¹,², Mehmet Sayiner¹, Leyla De Avila¹, Zahra Younoszai¹, Andrei Racila¹, Zobair M. Younossi*¹,³

USE of HCV graft in USA


2.9 3.3 5.8 6.8 9.4
The dilemma using anti-HCV+ liver grafts

Risk of transmission
Variable depending on:
• Quality of Screening
• Viral replication (& detection)
• HCV status of the recipient

Benefits for the recipients
• Higher chance for grafting
• Emergency liver transplantation
How to optimize the use of anti-HCV+ liver grafts?

Minimizing risks

- Selection of donors/recipient
- Controlling the risk
- Effective prophylaxis or treatment

Maximizing benefits
Selection of anti-HCV+ donors/recipient

• All donors are currently screened for HCV status
  – *ELISA testing is the gold standard* (*Se >99*)

• Anti-HCV+ donors are NOT routinely screened for:
  – HCV RNA positivity in sera *(NAT): availability?*
  – Genotype
    – Only 53%-57% have active viral replication compared to 60–80% of anti-HCV-positive individuals1-3

*Anti-HCV+ liver grafts are allocated to patients who consent to receive such organs and who have a HCV+ status*

Recipients with positive serology but with undetectable HCV RNA have theoretically a similar exposure risk than naive patients, as there is no protective cross-immunity between different inocula of HCV.

HCV(+) graft in HCV(+) recipients
Use of HCV(+) Grafts in HCV+ Recipients

Donor HCV status, donor age and outcome

**Graft**

- HCV (+), donor age < 50, n = 30
- HCV (+), donor age ≥ 50, n = 9
- HCV (-), donor age < 50, n = 320
- HCV (-), donor age ≥ 50, n = 260

**Patient**

- HCV (+), donor age < 50, n = 30
- HCV (+), donor age ≥ 50, n = 9
- HCV (-), donor age < 50, n = 320
- HCV (-), donor age ≥ 50, n = 260

Donor Age cut-off: 50 yrs
Use of HCV(+)

Grafts in HCV+ Recipients

<table>
<thead>
<tr>
<th>Variable</th>
<th>Without HCV (no.)</th>
<th>With HCV (no.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total patients</td>
<td>61,905</td>
<td>1,244</td>
</tr>
</tbody>
</table>

Non-adjusted

- $p = 0.001$
- $p = 0.01$

Adjusted

- $p = \text{ns}$
- $p = \text{ns}$
Use of HCV(+) Grafts in HCV+ Recipients

Case control Study n = 63 vs 63

No impact on survival
Use of HCV(+) Grafts in HCV+ Recipients

Case control Study n=63 VS 63

HCV recurrence-free survival.

Donor serology

Donor Histology Fibrosis >1
Use of HCV(+) Grafts in HCV+ Recipients

Donor HCV status, donor age and outcome

Donors < 45 yrs

Donors > 45 yrs

Mean donor age in Europe > 55 yrs !!!!
Use of HCV(+) Grafts in HCV+ Recipients

Montenovo et al, Ann Transplant 2015; 20: 44-50
**HCV Genotype «dominance»**

- This dominance is determined according to GT and not according to D or R status\(^1\)
- In 23 liver recipients, patients in whom the donor strain became predominant had significantly longer disease-free survival than patients who retained their own HCV strain\(^2\)

---

HCV(+) graft in HCV(-) recipients
Use of HCV + donors in HCV(-) Recipients

Of the 1,244 HCV(+) allografts, 369 were transplanted into HCV(-) recipients (30.7%).

A case-controlled cohort (11 donor and recipient variables): propensity scores with a matching algorithm (n = 540 in each group)

Adjusted

A Sub-analysis of the HCV(-) recipients receiving a HCV(+) graft is missing
Use of HCV + donors in HCV(-) recipients

193
R(-) / D(+)

Liver allografts from hepatitis C positive donors can offer good outcomes in hepatitis C positive recipients: a US National Transplant Registry analysis


193 R(-) / D(+)
Use of HCV + donors in HCV(-) recipients

<table>
<thead>
<tr>
<th>Recipient and transplant variables</th>
<th>Anti-HCV-positive graft (n=63)</th>
<th>Anti-HCV-negative graft (n=63)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>54.6 (±8.1)</td>
<td>55.7 (±8.1)</td>
<td>0.12</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>50 (79.4)</td>
<td>50 (79.4)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>13 (20.6)</td>
<td>13 (20.6)</td>
<td>1.00</td>
</tr>
<tr>
<td>ABO blood group</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Compatible</td>
<td>2 (3.2)</td>
<td>1 (1.6)</td>
<td></td>
</tr>
<tr>
<td>Isogroup</td>
<td>61 (96.8)</td>
<td>62 (98.4)</td>
<td>1.00</td>
</tr>
<tr>
<td>Real MELD score, mean (SD)</td>
<td>16 (±5.4)</td>
<td>16.2 (±5.0)</td>
<td>0.33</td>
</tr>
<tr>
<td>Associated hepatocarcinoma</td>
<td>35 (55.6)</td>
<td>41 (65.1)</td>
<td>0.36</td>
</tr>
<tr>
<td>Meeting Milan criteria</td>
<td>29 (82.9)</td>
<td>32 (78)</td>
<td>0.81</td>
</tr>
<tr>
<td>Meeting UCSF criteria</td>
<td>6 (17.1)</td>
<td>9 (22)</td>
<td></td>
</tr>
<tr>
<td>HBV co-infection</td>
<td>10 (15.9)</td>
<td>4 (6.3)</td>
<td>0.15</td>
</tr>
<tr>
<td>HCV-RNA recipient</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>61 (96.8)</td>
<td>56 (88.9)</td>
<td>0.16</td>
</tr>
<tr>
<td>Negative</td>
<td>2 (3.2)</td>
<td>7 (11.1)</td>
<td></td>
</tr>
</tbody>
</table>
Proposal to accept grafts from HCV infected donors

- **Anti HCV(+) D**
  - **HCV RNA(+) or unknown**
    - **Histological evaluation**
      - F0-F1: Accept
      - ≥F2: Reject

*adapted from Coilly, A and Samuel, D. J hepatol. 2015.*
HCV recurrence is curable

Post-LT SVR

- SOF/RBV: 70%
- SOF/SIM: 90%
- SOF/LDV: 95%
- SOF/DAC: 94%
- SOF/VEL: 97%
- 3D: 95%

PICO 4
Use of HCV + donors

- Coordinator: Mário Guimarães Pessôa
- Working Group: Michael Charlton (US), Stefano Fagiuoli (EU), James Fung (HK), John Roberts (USA)
Use of HCV(+) Grafts in HCV(+) Recipients: STATEMENTS

**Recommendation 5.1:**
We recommend the use of anti-HCV-positive grafts in antiHCV-positive, HCV-RNA-positive recipients.

Quality/Certainty of Evidence: Moderate
Strength of Recommendation: Strong

**Recommendation 5.2:**
We recommend against the use of grafts from donors with F2 fibrosis.

Quality/Certainty of Evidence: Moderate
Strength of Recommendation: Strong
Use of HCV(+) Grafts in HCV(+) Recipients: STATEMENTS

**Recommendation 5.3:**
We suggest a limited use of anti-HCV-positive grafts (HCV RNA-positive or unknown) in anti-HCV or HCV RNA negative recipients.

Quality/Certainty of Evidence: Very Low  
Strength of Recommendation: Conditional

**Recommendation 5.4:**
We recommend that liver transplant recipients of anti-HCV-positive grafts, with confirmed viremia after transplantation, be treated with antiviral therapy early.

Quality/Certainty of Evidence: Very Low  
Strength of Recommendation: Conditional
Persons who inject drugs (PWID) are anticipated to be the main source of HCV viremic donors in next decade.

National data suggests that currently there are ~300-500 additional (unrealized) opportunities for donation among HCV viremic PWID deaths and the trend line is increasing.
Renal transplantation

A large observational study from Spain that captured these data demonstrated that there was no difference in 10-year outcomes between recipients with HCV that received kidneys from HCV “positive” versus negative donors (28). Furthermore, by accepting an organ from an HCV “positive” donor, kidney transplant candidates may significantly shorten their waiting time depending on the geographic region.
Other Organ Transplants in HCV(+)

Thoracic transplantation

Lung survival rates were not significantly different for HCV-infected and uninfected recipients after 1999. Despite this, a 2011 survey of lung transplant programs found that <20% would transplant HCV viremic patients (34).

Heart This general avoidance of HCV-infected recipients is also seen in cardiac transplantation, perhaps due to pre-DAA data demonstrating inferior outcomes (12). There are very little data on the outcomes of HCV-negative recipients receiving thoracic organs from HCV “positive” donors.
HIV(+) Grafts
Outline

• Why HIV(+) grafts

• Epidemiology, Knowledge gaps, risks

• Clinical trials

• Recipient/Donor Selection

• Virologic consideration

• Organ Rejection Risk/Latent Opportunistic Infections
• **Life expectancy** among HIV-infected (HIV+) individuals has improved dramatically with effective ART.

• Chronic diseases such as End-stage liver and kidney diseases are growing causes of morbidity and mortality.

• HIV+ individuals can have **excellent outcomes after SOT** and the need for transplantation in this population is increasing.

• Due to a significant **organ shortage** HIV+ individuals experience high mortality rates on transplant waitlists.
FIGURE 1. The number of liver transplants performed among the general population and the number of liver transplants performed among HIV+ patients between 2002 and 2011.
US HIV D-/R+ transplant volumes

HIV+ Kidney Transplants

HIV+ Liver Transplants
Similar survival after LT in patients with and without HIV infection

- **HCV coinfection** (HR 7.79 [1.07-56])
- **Maximum nodule diameter >3 cm** (HR 1.72 [1.02-2.89])

were the variables associated with death

Hepatology. 2016;63:488-498
Liver Transplant in HIV(+)/HCV(+)
Interferon-free therapy is effective and safe for HCV recurrence in HCV/HIV LT recipients: the FIPSE cohort

N = 148 DAA
SVR in HIV- = 95%

N = 47 DAA
SVR in HIV+ = 94%
### Post-LT DAA Treatment in HIV(+) / HCV(+)

<table>
<thead>
<tr>
<th></th>
<th>SVR12 ITT (overall)</th>
<th>SVR12 mITT (overall)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SOF + RBV SVR ITT</strong></td>
<td>8/9 (^{3a}) (89%)</td>
<td>8/9 (^{3a}) (89%)</td>
</tr>
<tr>
<td><strong>SOF + RBV SVR mITT</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>SOF + DCV ± RBV ITT</strong></td>
<td>8/9 (^{4c}) (89%)</td>
<td>8/8 (100%)</td>
</tr>
<tr>
<td><strong>SOF + DCV ± RBV mITT</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>SOF/LDV ± RBV ITT</strong></td>
<td>6/6 (100%)</td>
<td></td>
</tr>
<tr>
<td><strong>SOF/LDV ± RBV mITT</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Outline

• Why HIV(+) grafts

• Epidemiology, Knowledge gaps

• Clinical trials

• Recipient/Donor Selection

• Virologic consideration

• Organ Rejection Risk/Latent Opportunistic Infections
### Estimated Risk of Human Immunodeficiency Virus and Hepatitis C Virus Infection among Potential Organ Donors from 17 Organ Procurement Organizations in the United States

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Risk status(^1)</th>
<th>N</th>
<th>Prevalence (%) for organ donors in study(^2)</th>
<th>Prevalence (%) blood donors(^3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV</td>
<td>Normal risk</td>
<td>11245</td>
<td>0.10</td>
<td>0.011 (0.008–0.013)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(0.06–0.16)</td>
<td></td>
</tr>
<tr>
<td>HIV</td>
<td>High risk</td>
<td>1180</td>
<td>0.50</td>
<td>0.011 (0.008–0.013)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(0.21–0.86)</td>
<td></td>
</tr>
<tr>
<td>HIV</td>
<td>Missing risk</td>
<td>1182</td>
<td>1.00</td>
<td>0.011 (0.008–0.013)</td>
</tr>
<tr>
<td></td>
<td>status</td>
<td></td>
<td>(0.57–1.54)</td>
<td></td>
</tr>
<tr>
<td>HIV</td>
<td>All potential</td>
<td>13607</td>
<td>0.21</td>
<td>0.011 (0.008–0.013)</td>
</tr>
<tr>
<td></td>
<td>donors</td>
<td></td>
<td>(0.15–0.29)</td>
<td></td>
</tr>
</tbody>
</table>

\(^1\)Source: Organ Procurement Organizations.  
\(^2\)Source: Organ Procurement Organizations.  
\(^3\)Source: CDC National Health and Nutrition Examination Surveys.
Clinical risk

Kidney

14-fold increase
Number Prevalent HIV+ ESKD patients (1999 to 2010)

Survival of HIV+ on Dyalisis is poor.
5-year survival:
• HIV+ 63%
• HIV- 94%

Liver

Increased waitlist mortality in HIV+
• 36% in HIV+.
• 15% in HIV- patients matched for MELD score
- Why HIV(+) grafts
- Epidemiology, Knowledge gaps
- Initial Clinical trials
- Recipient/Donor Selection
- Virologic consideration
- Organ Rejection Risk/ Latent Opportunistic Infections
Renal Transplantation between HIV-Positive Donors and Recipients

Table 1. Clinical Characteristics of HIV-Positive Recipients of a Transplant from an HIV-Positive Donor.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Patient 1</th>
<th>Patient 2</th>
<th>Patient 3</th>
<th>Patient 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>47</td>
<td>56</td>
<td>37</td>
<td>29</td>
</tr>
<tr>
<td>Sex</td>
<td>Male</td>
<td>Male</td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>Diagnosis on renal biopsy</td>
<td>HIV-associated nephropathy</td>
<td>HIV-associated nephropathy and hypertensive nephropathy</td>
<td>Malignant hypertension</td>
<td>HIV-associated nephropathy</td>
</tr>
<tr>
<td>Creatinine (μmol/liter)</td>
<td>678</td>
<td>582</td>
<td>1712</td>
<td>725</td>
</tr>
<tr>
<td>CD4 count (cells/mm³)</td>
<td>288</td>
<td>258</td>
<td>132</td>
<td>147</td>
</tr>
<tr>
<td>HIV viral load (copies/ml)</td>
<td>&lt;50</td>
<td>&lt;50</td>
<td>&lt;50</td>
<td>&lt;50</td>
</tr>
<tr>
<td>Antiretroviral regimen</td>
<td>Tenofovir, lamivudine, and lopinavir–ritonavir</td>
<td>Stavudine, lamivudine, and efavirenz</td>
<td>Stavudine, lamivudine, and nevirapine</td>
<td>Zidovudine, lamivudine, and nevirapine</td>
</tr>
</tbody>
</table>

Muller et al, NEJM 2010: 362: 2336-7
27 recipients
- CD4 > 200, VL < 50
- Median age 41
- 56% male
- 96% African
- 94% HIV-associated nephropathy

15 donors
- Median age 30
- Cause of death: trauma, overdose, SAH
- 14 treatment naïve, 1 on antiretroviral therapy
N = 27  South Africa: HIV-to-HIV

HIV disease and infections
- 100% HIV suppression maintained
- One case of extra-pulmonary TB, one of aspergillus

Rejection (all received ATG/thymoglobuline)
- 8% - 1 year
- 22% - 3 years

Recurrent HIV-AN?
- 3/27 early histologic changes with normal eGFR
Outline

• Why HIV(+) grafts

• Epidemiology, Knowledge gaps, risks

• Clinical trials

• **Recipient/Donor Selection**

• Virologic consideration

• Organ Rejection Risk/Latent Opportunistic Infections
National Organ Transplant Act, 1984/88

BAN !!!

42 U.S.C. 274(b) Sect 372(b):

“requires the OPTN to adopt and use standards for preventing the acquisition of organs from individuals known to be infected with HIV.”
Estimating the Potential Pool of HIV-Infected Deceased Organ Donors in the United States

B. J. Boyarsky\textsuperscript{a}, E. C. Hall\textsuperscript{a,b}, A. L. Singer\textsuperscript{a}, R. A. Montgomery\textsuperscript{a}, K. A. Gebo\textsuperscript{c,d,e} and D. L. Segev\textsuperscript{a,d,*}

\textsuperscript{a}Department of Surgery, Johns Hopkins School of Medicine, Baltimore, MD
\textsuperscript{b}Department of Surgery, Georgetown University School of Medicine, Washington, DC
\textsuperscript{c}Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, MD
\textsuperscript{d}Department of Epidemiology, Johns Hopkins School of Public Health, Baltimore, MD
\textsuperscript{e}HIV Research Network, Baltimore, MD

\textsuperscript{*}Corresponding author: Dorry L. Segev, dorry@jhmi.edu

\begin{itemize}
  \item 2000-2008
  \item 2 national registries (NIS, HIVRN)
  \item Excluded those with missing data and medical contraindication
  \item \textbf{500-600 donors per year}
\end{itemize}
Since organs from HIV+ donors could fill a critical need, the HIV Organ Policy Equity (HOPE) Act was passed in November 2013, reversing the federal ban on the use of HIV+ donors for HIV+ recipients.
Learn if the use of HIV+ deceased donors is safe and effective in the US
HIV+ Candidate Inclusion Criteria

- No active opportunistic infections or cancer
- **Kidney** CD4 > 200 cells
- HIV RNA suppressed on effective ART
- **Liver** CD4 > 100 cells
  - If unable to tolerate ART, an effective regimen is anticipated post-transplant
HIV Donor+ Inclusion Criteria

National Institute of Allergy and Infectious Diseases (NIAID) initial draft of minimum eligibility criteria for HIV-infected organ donation via a research protocol

<table>
<thead>
<tr>
<th></th>
<th>Deceased donor</th>
<th>Living donor</th>
</tr>
</thead>
<tbody>
<tr>
<td>New HIV infection diagnosis</td>
<td>≥200</td>
<td>≥200</td>
</tr>
<tr>
<td>History of HIV infection</td>
<td>≥500 for 6 months prior to organ procurement</td>
<td></td>
</tr>
<tr>
<td>CD4 count (cells/mm³)</td>
<td>≥200</td>
<td>≥200</td>
</tr>
<tr>
<td>HIV VL (copies/mL)</td>
<td>No requirement</td>
<td>≤50</td>
</tr>
<tr>
<td>Antiretroviral resistance</td>
<td>≤1 antiretroviral class</td>
<td>≤1 antiretroviral class</td>
</tr>
<tr>
<td>Opportunistic infection</td>
<td>None active</td>
<td>None active</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>≤1 antiretroviral class</td>
</tr>
<tr>
<td></td>
<td></td>
<td>None active</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No history of:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Chronic cryptosporidiosis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CNS lymphoma</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Progressive multifocal leukoencephalopathy</td>
</tr>
</tbody>
</table>

<sup>a</sup>Odim J. The HOPE Act: criteria for transplanting kidneys or livers from HIV+ donors into HIV+ recipients. Oral presentation at 54th Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC). 2014; Washington, DC
HIV+ kidney or liver transplant candidates

Consented for study
N = 155

Received transplant
N = 41

HIV- donors = 16
HIV false positive donors = 6
HIV D-/R+ transplants N = 30 (15)

21 kidneys (11)
*3 SLKs

6 livers (5)
*3 SLKs

HIV+ donors N = 5
HIV D+/R+ transplants N = 11

8 kidneys

3 livers

ClinicalTrials.gov: NCT02602262
HOPE: Post-transplant outcomes

Among those who received kidneys:

Log-rank p-value = 0.2

Among those who received livers:

Log-rank p-value = 0.5
Outline

• Why HIV(+) grafts

• Epidemiology, Knowledge gaps, risks

• Clinical trials

• Recipient/Donor Selection

• Virologic consideration

• Organ Rejection Risk / Latent Opportunistic Infections
HIV Superinfection

- Transmission of a second distinct HIV strain from Donor to Recipient
- Observed in ALL models of HIV transmission (*IVDU, Sex*)
- Rates similar to Primary Infection

Unknown in Organ Transplant
HIV Tropism

Refers to the cellular co-receptor to which HIV binds in the initial steps of infection

R5 Tropic (to CCR5 Chemokine Receptor)
- Most Common
- Maraviroc (MVC) active

X4 Tropic (to CXCR4 Chemokine Receptor)
- In 50% of <200 cells/uL / Late stage
- MVC not active
- Associated with accelerated progression

Common commercial tests: 1 week !!

History of ART needs to be recorded in Donor
ART Resistance

- **Primary**: Refers to Donor – Recipient Transmission
- **Secondary**: Through Drug selection pressure on ART when viral suppression not achieved or maintained

Possible impact on recipient!!!

History of ART needs to be recorded in Donor
Outline

• Why HIV(+) grafts
• Epidemiology, Knowledge gaps, risks
• Clinical trials
• Recipient/Donor Selection
• Virologic consideration
• Organ Rejection Risk / Latent Opportunistic Infections
HIV+ liver grafts

TABLE 1.
Patient characteristics by HIV status

<table>
<thead>
<tr>
<th></th>
<th>HIV+ (n = 180)</th>
<th>HIV- (n = 34,020)</th>
<th>P</th>
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</thead>
<tbody>
<tr>
<td>Pretransplant GFR</td>
<td></td>
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<tr>
<td>≥ 90</td>
<td>32.8</td>
<td>28.8</td>
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<tr>
<td>60-89</td>
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<tr>
<td>30-59</td>
<td>26.7</td>
<td>26.7</td>
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<tr>
<td>15-29</td>
<td>7.8</td>
<td>9.8</td>
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<tr>
<td>&lt; 15</td>
<td>3.3</td>
<td>3.7</td>
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<tr>
<td>MELD score, median (IQR)</td>
<td>19 (12.5-29)</td>
<td>19 (13-27)</td>
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<tr>
<td>HCV infection</td>
<td>64.9</td>
<td>45.8</td>
<td>&lt;0.001</td>
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<tr>
<td>HBV infection</td>
<td>64.1</td>
<td>22.7</td>
<td>&lt;0.001</td>
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<tr>
<td>Acute rejection within 1 y</td>
<td>16.1</td>
<td>12.1</td>
<td>0.09</td>
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<tr>
<td>Donor characteristics</td>
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<tr>
<td>Age ≥ 50 y</td>
<td>34.4</td>
<td>36.7</td>
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<tr>
<td>Race</td>
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<tr>
<td>African American</td>
<td>21.7</td>
<td>17.2</td>
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<tr>
<td>White</td>
<td>60.0</td>
<td>67.2</td>
<td>0.12</td>
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<tr>
<td>Other</td>
<td>18.3</td>
<td>15.7</td>
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<tr>
<td>CIT ≥ 6 h</td>
<td>64.1</td>
<td>63.3</td>
<td>0.82</td>
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## HOPE: Post-transplant outcomes

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<tr>
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<th>HIV D-/R+</th>
<th>HIV D+/R+</th>
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<tbody>
<tr>
<td></td>
<td>N=30</td>
<td>N=11</td>
</tr>
<tr>
<td>Rejection episodes; N (%)</td>
<td>4 (13.3%)</td>
<td>3 (27.3%)</td>
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<tr>
<td>Opportunistic Infections; N (%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
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<tr>
<td>Breakthrough viremia; N (%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
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<tr>
<td>Malignancy; N (%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
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<tr>
<td>Graft failure; N (%)</td>
<td>0 (0%)</td>
<td>1 (9.1%)</td>
</tr>
<tr>
<td>Death; N (%)</td>
<td>0 (0%)</td>
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</table>
Standard donor criteria plus positive HIV ELISA and/or NAT*

Undetectable HIV (RNA <200 c/mL)
- Antiretroviral treatment
- Lower risk of HIV superinfection and drug resistance

Detectable HIV (RNA >200 c/mL)
- Antiretroviral treatment naïve
- Virologic failure on antiretrovirals
- Higher risk of HIV superinfection and drug resistance

Potential HIV(+) D
- First line ART regimen
- R5 tropic virus
- Potential for PI Ritonavir-sparing regimen
- Higher CD4+ T cell count

- Second-line ART
- X4 tropic virus
- History of drug resistance
- Requires PI/Ritonavir-based regimen
- Lower CD4+ T cell count

Boyarsky, Durand, Segev AJT in press
A Journey of a thousand miles begins with a single step

Chinese saying
Grazie dell’attenzione
### Use of HCV + Grafts

**1. HCV D+/R+ VS HCV D-/R+**

**AIM:** evaluation of overall survival (OS) and graft survival (GS) in HCV + R who received either HCV + or - allograft

<table>
<thead>
<tr>
<th>Authors</th>
<th>D+/R+ (n)</th>
<th>D-/R+ (n)</th>
<th>OS 1 y</th>
<th>OS 2y</th>
<th>p</th>
<th>GS 1 y</th>
<th>GS 2 y</th>
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<td>D-/R+</td>
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<tr>
<td>Marroquin</td>
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<td>Ricchiuti</td>
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<td>NSp*</td>
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<td>Alvaro</td>
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<td>130</td>
<td>91.7%</td>
<td>83%</td>
<td>80%</td>
<td>70%</td>
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<td>Stepanova</td>
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</table>

*NSp: not specified in the text. Citation: “cumulative five years OS and GS not significantly differ”

**NSp**: not specified in the text. Citation: “Both mortality rate and graft los in HCV patients transplanted from HCV + donors were similar to those in HCV pts transplanted from HCV neg donors (all p >0.05)”