European Experience in Liver Transplantation in HIV-infected patients

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- 8,500 patients (historical cohort)
- 5,000 active patients
- 4,800 on cART (>90% VL BDL)
- 27% HCV coinfection
- 6% HBV coinfection
- ESLD first cause of death in HCV/HIV coinfected patients
HIV-infected patients with ESOD are routinely evaluated for SOT
Multidisciplinary approach
Prospective evaluation
Evaluation for Liver, Kidney, and Heart Transplantation of Spanish HIV-1–Infected Patients With ESOD
Hosp. Clinic, Barcelona (Spain) between 2000-2017

<table>
<thead>
<tr>
<th>Procedure</th>
<th>No. patients / No. admitted WL</th>
<th>No. who underwent transplant</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Liver transplantation</strong></td>
<td>290 / 75</td>
<td>32 (11%)</td>
</tr>
<tr>
<td><strong>Kidney (Pancreas) transplantation</strong></td>
<td>30 (3) / 24 (3)</td>
<td>15 (1) (50%)</td>
</tr>
<tr>
<td><strong>Heart transplantation</strong></td>
<td>4 / 3</td>
<td>3</td>
</tr>
</tbody>
</table>
European Experience in LT in HIV-infected Patients

Outline

• HIV inclusion criteria for LT
• Natural history of liver transplantation
• Anti-HCV Therapy. Role DAA
• Antiretroviral therapy
• Concluding remarks
### HIV Criteria for SOT: European and U.S. Recommendations

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Spain</th>
<th>Italy</th>
<th>U.K.</th>
<th>U.S.A.</th>
</tr>
</thead>
<tbody>
<tr>
<td>C events</td>
<td>Some*</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>- OIs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Neoplasms</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CD4 count</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- OLT</td>
<td>&gt;100</td>
<td>&gt;200</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Other SOT</td>
<td>&gt;200</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VL BDL**</td>
<td>Yes</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Spain: TB, PCP or candidiasis; USA: Only PML, cryptosporidiosis, MDR fungal Infections, NHL and vKS are exclusion criteria.

** If VL was detectable, post-OLT suppression predicted in all cases.

* DC=Decompensated cirrhosis; PHT: portal hypertension.

2018 Guidelines will include a section of SOT in HIV-infection as part of routine clinical care
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• Antiretroviral therapy
• Concluding remarks
FIPSE-Funded Clinical Trial: 
*Liver Transplantation (N=250)*
*in Spanish HIV-Infected Patients*
*at 23 Spanish Transplant Centers (2002-12)*

**PI:** José M. Miró (H. Clinic, Barcelona, Spain)  
**Co-PI:** Spanish Transplant Centers  
**AEC-GESIDA / GESITRA (SEIMC)**  
**SETH / ONT / SPNS (MSC)**
Models of OLT in HIV Infected Patients

- **USA**: NIH-Trial in selected sites
- **E.U. countries**: selected sites
- **Spain**: All sites (N=275 cases & 825 controls)
Outcome of HCV/HIV-Coinfected Liver Transplant Recipients: A Prospective and Multicenter Cohort Study

J. M. Miro⁠, M. Montejo⁠, L. Castells⁠, A. Rafecas⁠, S. Moreno⁠, F. Agüero⁠, M. Abradelo⁠, P. Miralles⁠, J. Torre-Cisneros⁠, J. D. Pedreira⁠, E. Cordero⁠, G. de la Rosa⁠, B. Moyano⁠, A. Moreno⁠, I. Perez⁠, A. Rimola and the Spanish OLT in HIV-Infected Patients Working Group investigators†

with <1 liver transplantation/year in HIV-infected patients) that allowed us to identify a subset of 60 (71%) patients with a similar 5-year prognosis (69% [95% CI, 54–80]) to that of HCV-monoinfected recipients. In conclusion, 5-year survival in HCV/HIV-coinfected liver recipients was lower than in HCV-monoinfected liver recipients, although an important subset with a favorable prognosis was identified in the former.

Key words: HCV infection, HIV infection, Liver Transplantation, Spain, Survival

Abbreviations: AIDS, acquired immunodeficiency
Case (N=84) - Control (N=252) Study: Survival After OLT in HCV-Infected Patients According to HIV Status

- **HCV mono-infected**
  - 90% (86-93%)
  - 88% (79-93%)
  - 72% (66-77%)
  - 54% (42-64%)

- **HCV/HIV co-infected**
  - p = 0.0254

Patients at risk:
- HIV - 252
- HIV + 84

Years:
- 0
- 1
- 2
- 3
- 4
- 5

Survival Distribution Function
## Cause of Death in HCV-infected LT Recipients

**Spanish prospective, multicenter, cohort study (FIPSE Study)**

Preliminary results (2002-2006; end of follow-up: 2010)

<table>
<thead>
<tr>
<th>Cause of death</th>
<th>HCV/HIV (n = 84)</th>
<th>HCV (n = 252)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCV recurrence</td>
<td>18 (21%)</td>
<td>31 (12%)</td>
<td><strong>0.049</strong></td>
</tr>
<tr>
<td>Infection</td>
<td>7 (8%)</td>
<td>15 (6%)</td>
<td>NS</td>
</tr>
<tr>
<td>Tumors</td>
<td>3 (4%)</td>
<td>4 (2%)</td>
<td>NS</td>
</tr>
<tr>
<td>Technical problems</td>
<td>0</td>
<td>6 (2%)</td>
<td>NS</td>
</tr>
<tr>
<td>Other</td>
<td>8 (10%)</td>
<td>19 (8%)</td>
<td>NS</td>
</tr>
</tbody>
</table>

Miro JM on behalf FIPSE. Am J Transpl; 2012; 12:1866-76
### RESULTS

**Predictors of post-OLT mortality in HCV/HIV co-infected patients**

**All variables: pre-, peri-, and post-OLT**

<table>
<thead>
<tr>
<th>Predictor</th>
<th>p</th>
<th>Hazard ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCV genotype 1</td>
<td>0.008</td>
<td>2.98 (1.32-6.76)</td>
</tr>
<tr>
<td>Donor risk index</td>
<td>&lt;0.001</td>
<td>9.48 (2.75-32.73)</td>
</tr>
<tr>
<td>Negative plasma HCV RNA viral load at any time (before or after OLT)</td>
<td>0.009</td>
<td>0.14 (0.03-0.62)</td>
</tr>
</tbody>
</table>

Recipient age, gender, BMI, CD4, MELD & Child scores, HBV coinfection, Center with <1 OLT in HIV-infected patients/year, donor age, non-cranial trauma as cause of donor brain death, acute and chronic rejection, SVR to anti-HCV Rx, Pre-OLT and post-OLT peak HCV viral load, severe infection, invasive fungal infection and HCC were not associated with death.

# RESULTS

Predictors of post-OLT mortality in HCV/HIV co-infected patients

**Only Pre-OLT variables**

| Predictor                                         | p value | Hazard ratio  
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-OLT MELD score</td>
<td>0.023</td>
<td>1.06 (1.02-1.11)</td>
</tr>
<tr>
<td>Center with &lt;1 OLTs in HIV+/year</td>
<td>0.009</td>
<td>2.82 (1.30-6.94)</td>
</tr>
<tr>
<td>HCV genotype 1</td>
<td>0.029</td>
<td>2.27 (1.09-4.76)</td>
</tr>
</tbody>
</table>

**Risk score for mortality** = \( \exp \left[ 0.81966 \times \text{if HCV Genotype 1} + 0.05748 \times \text{Pre-OLT MELD} + 1.03540 \times \text{if Center < 1 OLT in HIV+/year} \right] \)

Post-OLT Survival in HCV/HIV Co-infected Patients According to their Risk Score (RS) for Mortality

According to their Risk Score (RS) for Mortality

- **Low Risk**
  - RS ≤ 1.077
  - N=60
  - 93% (83-97%)

- **High Risk**
  - RS > 1.077
  - N=24
  - 17% (5-35%)

NIH TRIAL
150 Kidney and 125 Liver Transplants

NORTHEAST
Baltimore, MD
Johns Hopkins (K,L)
University of Maryland (K)
Boston, MA
Beth Israel Deaconess Medical Center (K, L)
New York, NY
Mt. Sinai School of Medicine (K, L, Peds K)
Columbia University (L, Peds L)
Philadelphia, PA
Drexel University (L)
University of Pennsylvania (K, L)
Pittsburgh, PA
University of Pittsburgh (K, L)
Washington, D.C.
Washington Hospital Center (K)
Georgetown Medical Center (K, L)

WEST
San Francisco, CA
University of California, SF (K, L, Peds K, Peds L)
Los Angeles, CA
Cedars-Sinai (L)

MID-WEST
Chicago, IL
University of Chicago (K, L, Peds K, Peds L)
Rush University (K, L)
Northwestern (K, L)
Cincinnati, OH
University of Cincinnati (K, L)
Cleveland, OH
Cleveland Clinic (K, L)

SOUTHEAST
Atlanta, GA
Emory University (K)
Charlottesville, VA
University of Virginia (K,L)
Miami, FL
University of Miami (K)
New Orleans, LA
Tulane (K, L, Peds K, Peds L)
Preliminary HCV-HIV Analysis

- HCV-HIV co-infected (n=81) vs HCV mono-infected (n=213)
  - Controls: HCV mono-infected recipients matched on study site; single vs dual organ transplant; HCC

- Predictors of patient and graft survival

Terrault et al, Liver Transplantation. 2012
Patient Survival: HCV

**HCV mono-infected**
- N=135
- N=67
- N=22

**HCV-HIV co-infected**
- N=46
- N=28
- N=14

\[ P = 0.01 \]
## Mortality Predictors in HCV/HIV co-infected Recipients in USA

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Hazard Ratio (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dual Kidney-Liver</td>
<td>5.5 (1.8, 16.9)</td>
<td>0.003</td>
</tr>
<tr>
<td>HCV+ Donor</td>
<td>4.5 (1.8, 11.2)</td>
<td>0.001</td>
</tr>
<tr>
<td>BMI at Listing &lt;21</td>
<td>2.7 (1.0, 7.3)</td>
<td>0.05</td>
</tr>
<tr>
<td>Treated Acute Rejection</td>
<td>2.9 (1.2, 7.0)</td>
<td>0.02</td>
</tr>
</tbody>
</table>

Terrault et al, Liver Transplantation. 2012
Cumulative Patient Survival at 5 yr. in HIV-HCV Infected LT Recipients in the pre-DAA era

Survival of OLT in HCV/HIV-Coinfected Recipients in the pre-DAA era

Lower than HIV-negative recipients but still acceptable
Is liver transplantation (LT) feasible in HIV-infected patients with hepatocellular carcinoma (HCC)?

Limited data
Human Immunodeficiency Virus Infection Does Not Worsen Prognosis of Liver Transplantation for Hepatocellular Carcinoma

Fernando Agüero,1 Alejandro Forner,2,3 Christian Manzardo,1 Andres Valdivieso,4,5 Marino Blanes,6 Rafael Barcena,7 Antoni Rafecas,8 Lluis Castells,3,9 Manuel Abradelo,10 Julian Torre-Cisneros,11 Luisa Gonzalez-Díezuez,12 Magdalena Salcedo,13 Trinidad Serrano,14 Miguel Jimenez-Perez,15 Jose Ignacio Herrero,3,16,17 Mikel Gastaca,4,5 Victoria Aguilera,3,6 Juan Fabregat,8 Santos del Campo,7 Itxarone Bilbao,9 Carlos Jimenez Romero,10 Asuncion Moreno,1 Antoni Rimola,3,18 Jose M. Miro1 and the FIPSE Investigators

Hepatology. 2016;63:488-498
Similar HCC recurrence in LT recipients with and without HIV infection

Microscopic vascular invasion was the only variable associated with HCC recurrence
HR (95% CI) 3.40 (1.34-8.64)
Similar survival after LT in patients with and without HIV infection

HCV coinfection (HR 7.79 [1.07-56]) and maximum nodule diameter >3 cm (HR 1.72 [1.02-2.89]) were the variables associated with death.
Is liver retransplantation (reLT) feasible in HIV-infected recipients?

Limited data
Liver Retransplantation in HIV-Infected Patients: A Prospective Cohort Study


*Hospital Universitario de Cruces, University of the Basque Country, Bilbao, Spain
bTraining Unit in Preventive Medicine and Public Health, Parc de Salut Mar-UPF-ASPB, Barcelona, Spain
cHospital Clínico-IDIBAPS, University of Barcelona, Barcelona, Spain
dCIBEREHD, Spain
eHospital General Universitario Gregorio Marañón, Madrid, Spain
fHospital Clínico Universitario Lozano Blesa, Zaragoza, Spain

transplantation showed better 3-year survival probability (80% and 67%, respectively), similar to that in their respective HIV-negative counterparts (72% and 70%). In HIV-infected and HIV-negative patients, 3-year survival probability in those with positive HCV RNA at retransplantation was 22% versus 65% (p = 0.008); in those with early retransplantation, 3-year survival probability was 25% versus 56% (p = 0.282). HIV infection was controlled with antiretroviral therapy after retransplantation. In conclusion, HIV-infected patients taken as a whole have unsatisfactory survival after liver retransplantation, although patients with undetectable HCV RNA at retransplantation or undergoing late retransplantation show a more favorable outcome.

Key words: Chronic rejection, HBV infection, HCV infection, HCV recurrence, HIV infection, liver retransplantation, primary- graft nonfunction, Spain, survival, vascular thrombosis.
Probability of survival after reLT in HIV-infected Recipients


<table>
<thead>
<tr>
<th>Months</th>
<th>0</th>
<th>1</th>
<th>3</th>
<th>12</th>
<th>24</th>
<th>36</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV -</td>
<td>157</td>
<td>126</td>
<td>108</td>
<td>87</td>
<td>68</td>
<td>52</td>
</tr>
<tr>
<td>HIV+</td>
<td>14</td>
<td>13</td>
<td>11</td>
<td>6</td>
<td>4</td>
<td>3</td>
</tr>
</tbody>
</table>

p-value=0.16

64%
42%
Probability of survival in patients with negative HCV RNA (B) and in positive HCV RNA (C) at reLT

<table>
<thead>
<tr>
<th>Country</th>
<th>Primary LT</th>
<th>reLT (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spain</td>
<td>270</td>
<td>14 (5)</td>
</tr>
<tr>
<td>USA</td>
<td>125</td>
<td>9 (7)</td>
</tr>
<tr>
<td>Italy</td>
<td>118</td>
<td>5 (4)</td>
</tr>
<tr>
<td>Germany</td>
<td>30</td>
<td>4 (13)</td>
</tr>
<tr>
<td>UK</td>
<td>24</td>
<td>2 (8)</td>
</tr>
<tr>
<td>Argentina</td>
<td>10</td>
<td>1 (11)</td>
</tr>
<tr>
<td>Portugal</td>
<td>13</td>
<td>1 (8)</td>
</tr>
<tr>
<td>Switzerland</td>
<td>10</td>
<td>1 (10)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>600</strong></td>
<td><strong>37 (6)</strong></td>
</tr>
</tbody>
</table>
Overall patient survival rate after reLT

Kaplan-Meier survival estimate

51% (34,65)

Patient survival rates according to HCV RNA status at reLT

The indication for reLT in HCV-HIV LT recipients should be reassessed in the era of DAA

European Experience in LT in HIV-infected Patients

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• HIV inclusion criteria for LT
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What is the efficacy of Peg-INF plus RBV for treating recurrent HCV after OLT in HIV/HCV-coinfected recipients?

Very low for HCV GT 1/4

Limited data with DAAs
Peg-INF+RBV was started in 39 of 89 HCV-HIV OLT recipients (44%).

Rates of SVR according to HCV genotypes:

**Modified ITT analysis**

<table>
<thead>
<tr>
<th>Overall</th>
<th>Genotype 1</th>
<th>Genotype Non-1</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=37</td>
<td>N=31</td>
<td>N=6</td>
</tr>
<tr>
<td>5 (14%)</td>
<td>3 (10%)</td>
<td>2 (33%)</td>
</tr>
</tbody>
</table>

SVR = Sustained response.

Spanish Cohort (Castells L, J Hepatol, 2015)

HIV/HCV+  
N=149

- No HCV treatment  
n=65 (44%)
- HCV treatment  
N=84 (56%)*
  - Only INF n=3
  - Classic INF+RBV=1
  - Ongoing n=2

N=78  
- Finished 48-week therapy n=34 (44%)
- Premature discontinuation  n=44 (56%)**
  - Toxicity, n=17 (22%)***
  - Lack of efficacy, n=20 (26%)
  - Death, n=5 (6%)
  - Other, n=2 (2%)

HCV+  
N=447

- No HCV treatment  
n=240 (54%)
- HCV treatment  
N=207 (46%)*
  - Ongoing n=31

N=176  
- Finished 48-week therapy n=107 (61%)
- Premature discontinuation  n=69 (39%)**
  - Toxicity, n=19 (11%)***
  - Lack of efficacy, n=37 (21%)
  - Death, n=4 (2%)
  - Other, n=2 (1%)
  - Unknown, n=7 (4%)

*P=0.042; ** P=0.016; ***P=0.034
Virological Response (II)

SVR according to genotype

Genotype 1
- HIV/HCV: 10
- HCV: 33
- * p = 0.0079

Genotypes 2/3
- HIV/HCV: 59
- HCV: 80

Genotype 4
- HIV/HCV: 7
- HCV: 0

Castells L et al. J Hepatol. 2015; 62: 92–100
Survival After Anti-HCV Therapy

HCV-monoinfected patients

HCV/HIV-coinfected patients

Castells L et al. J Hepatol. 2015; 62: 92–100
What is the efficacy of therapy with new DAAs for treating recurrent HCV infection after OLT in HCV-monoinfected recipients?

It seems similar to that seen in HIV-negative recipients.
Studies with Sofosbuvir-based anti-HCV Therapy to Treat HCV Recurrence in HCV/HIV LT Recipients

<table>
<thead>
<tr>
<th>Location</th>
<th>N. cases</th>
<th>Fibrosis stage</th>
<th>SVR12 rates</th>
</tr>
</thead>
<tbody>
<tr>
<td>US, single center(^1)</td>
<td>9</td>
<td>(\leq F2)</td>
<td>87.5%</td>
</tr>
<tr>
<td>Europe, multicenter(^2)</td>
<td>20</td>
<td>F3/F4</td>
<td>89%</td>
</tr>
<tr>
<td>Spain, single center(^3)</td>
<td>11</td>
<td>F3/F4</td>
<td>100%</td>
</tr>
</tbody>
</table>

Treatment of severe recurrent HCV after LT in HIV-infected patients using Sofosbuvir-based therapy*


Table 2 | Response (HCV RNA <25 IU/mL) during and after treatment

<table>
<thead>
<tr>
<th></th>
<th>Overall (n = 20)</th>
<th>Early severe recurrence (n = 9)</th>
<th>Compensated and decompensated cirrhosis (N = 11)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>During treatment, n (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At week 4</td>
<td>14/20 (70)</td>
<td>5/9 (56)</td>
<td>9/11 (82)</td>
<td>0.20</td>
</tr>
<tr>
<td>At week 12</td>
<td>18/18 (100)</td>
<td>9/9 (100)</td>
<td>9/9 (100)</td>
<td>NA</td>
</tr>
<tr>
<td>At week 24</td>
<td>12/12 (100)</td>
<td>6/6 (100)</td>
<td>6/6 (100)</td>
<td>NA</td>
</tr>
<tr>
<td><strong>In post-treatment follow-up, n (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At week 12 (SVR12)</td>
<td>16/18 (89)</td>
<td>7/9 (78)</td>
<td>9/9 (100)</td>
<td>0.13</td>
</tr>
</tbody>
</table>

* SVR≈90%

*HCV RNA <25 IU/mL response during treatment is in patients for whom HCV-RNA results are available.

HCV LLOQ: <25 UI/mL.

† One patient died and one underwent LT during the study and were not included in the efficacy analysis, both with decompensated cirrhosis.

*SOF+RBV, 11; SOF+DCV+RBV, 5; SOF+SIM+RBV, 3 and SOF+RBV+Peg-INF 1 case.

Sofosbuvir was given a median time of 24 weeks.
SVR was associated with an improvement of laboratory test scores over time in LT HIV-infected recipients

Interferon-free therapy is effective and safe for HCV recurrence in HCV/HIV LT recipients: the FIPSE cohort

750 HIV -

250 HIV +

SVR in HIV- = 95%

SVR in HIV+ = 94%
European Experience in LT in HIV-infected Patients

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### Initial Combination Regimen for ART-naïve Adult HIV-positive Persons

**A) Recommended regimens (one of the following to be selected)**

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Dosing</th>
<th>Food requirement</th>
<th>Caution</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>2 NRTIs + INSTI</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ABC/3TC/DTG(i, ii)</td>
<td>ABC/3TC/DTG 600/300/50 mg, 1 tablet qd</td>
<td>None</td>
<td>Al/Ca/Mg-containing antacids should be taken well separated in time (minimum 2h after or 6h before).</td>
</tr>
<tr>
<td>TDF/FTC(iii, iv) + DTG</td>
<td>TDF/FTC 300^{(vii)}/200 mg, 1 tablet qd + DTG 50 mg, 1 tablet qd</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td><strong>Dolutegravir</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TDF/FTC/EVG/c(iii, iv, v)</td>
<td>TDF/FTC/EVG/c 300^{(vii)}/200/150/150 mg, 1 tablet qd</td>
<td>With food</td>
<td>Al/Ca/Mg-containing antacids should be taken well separated in time (minimum 2h after or 6h before).</td>
</tr>
<tr>
<td><strong>Elvitegravir</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TDF/FTC(iii, iv) + RAL</td>
<td>TDF/FTC 300^{(vii)}/200 mg, 1 tablet qd + RAL 400 mg, 1 tablet bid</td>
<td>None</td>
<td>Al/Ca/Mg-containing antacids should be taken well separated in time (minimum 2h after or 6h before).</td>
</tr>
<tr>
<td><strong>2 NRTIs + NNRTI</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TDF/FTC/RPV^{(iii)}</td>
<td>TDF/FTC/RPV 300^{(vii)}/200/25 mg, 1 tablet qd</td>
<td>With food (min 390 Kcal required)</td>
<td>Only if CD4 count &gt;200 cells/µL and HIV VL &lt;100,000 copies/mL. PPI contraindicated; H2 antagonists to be taken 12h before or 4h after RPV.</td>
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<tr>
<td><strong>Rilpivirine</strong></td>
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<tr>
<td>TDF/FTC(iii, iv) + DRV/r</td>
<td>TDF/FTC 300^{(vii)}/200 mg, 1 tablet qd + DRV 800 mg, 1 tablet qd</td>
<td>With food</td>
<td>Monitor in persons with a known sulfonamide allergy.</td>
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http://www.eacsociety.org, free App
Raltegravir-based ART Avoids PK Interactions Between Immunosuppressants and ARTs

- **Raltegravir***-based cART (2 NUCs)
  - Preliminary experience in 13 patients (OLT, 8; RT, 5)
  - No DDIs between RAL and CsA, FK and Sirolimus
  - No episodes of acute rejection

- **Maraviroc****-based cART (2 NUCs)

- **Enfuvirtide**-based cART (3 NUCs)

*and probably Dolutegravir; **Maraviroc has anti-rejection properties.
Drug–Drug Interactions (DDI) of IS with ARVs

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<th>DRV/c</th>
<th>DRV/c</th>
<th>LPV/r</th>
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<th>ETV</th>
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Legend:
↑ = potential increased exposure of the immunosuppressant; ↓ = potential decreased exposure of the immunosuppressant; * = no significant effect
D = potential decreased exposure of ARV drug; E = potential elevated exposure of ARV drug.
ATV/c = atazanavir coformulated with cobicistat (300/150 mg QID); DRV/c = darunavir coformulated with cobicistat (800/150 mg QID)
* available as prolonged release formulation
Numbers refer to decreased/increased AUC of the immunosuppressant as observed in drug–drug interaction studies
a = TDM of immunosuppressant is recommended; b = monitor renal function
AM = antimetabolite; CNI = calcineurin inhibitors; CS = corticosteroids; mTOR = mTOR inhibitors

Colors legend:
- no clinically significant interaction expected
- these drugs should not be coadministered
- potential clinically significant interaction that is likely to require additional monitoring, alteration of drug dosage or timing of administration
- potential interaction likely to be of weak intensity. Additional action/monitoring or dosage adjustment is unlikely to be required
Drug–Drug Interactions (DDI) of DAAs with ARVs

<table>
<thead>
<tr>
<th>Hepatitis C Directly Acting Antivirals (DAAs)</th>
<th>Daclatasvir</th>
<th>Ledipasvir/Sofosbuvir</th>
<th>OBV/PTVr + DSV</th>
<th>Simeprevir</th>
<th>Sofosbuvir</th>
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<td>OBV/PTVr + DSV</td>
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<th>OBV/PTVr + DSV</th>
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<th>Ledipasvir/Sofosbuvir</th>
<th>OBV/PTVr + DSV</th>
<th>Simeprevir</th>
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Potential for ledipasvir (LDV)-mediated increase in tenofovir levels, especially if tenofovir used with RTV. Avoid LDV if CrCl < 60 mL/min or if receiving tenofovir with RTV-boosted PI.
European Experience in LT in HIV-infected Patients

Outline

• HIV inclusion criteria for LT
• Natural history of liver transplantation
• Anti-HCV Therapy: Role DAA
• Antiretroviral therapy
• Concluding remarks
Conclusions

• LT evaluation in HIV-infected patients with ESLD is currently part of routine clinical care.

• Survival of LT in HIV/HCV-coinfected recipients with SVR treated with Peg-INF plus RBV is 80% at 5-yr and similar to that seen in HCV monoinfected recipients.

• SVR rates in HCV/HIV LT recipients with INF-free regimens are >90% and similar to that seen in HCV monoinfected patients.

• LT is effective for HIV-infected patients with HCC.

• But … there are new challenges in this field …
New Challenges in Liver Transplantation in HIV-infected Patients

- Long-term (10 yr.) outcomes in SVR
- Cancer de novo risk
- Predictors of acute rejection
- Best ART regimen (DTG*, MVC**, TAF)
- HIV D+ / R+ Transplantation

*3TC+Dolutegravir; **Maraviroc has anti-rejection properties.
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<td>3.433</td>
<td>147</td>
<td>56</td>
<td>&lt;50</td>
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</tbody>
</table>

From Week 8 onwards all patients had pVL < 50 copies/mL.
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