Hepatitis C plus HIV: How bad is it?

Pedro Cahn
Fig 1. Number of deaths due to major communicable diseases in 2013 [4]. Viral hepatitis deaths include those related to acute viral hepatitis, liver cancer secondary to hepatitis B and hepatitis C, and cirrhosis of the liver secondary to hepatitis B and hepatitis C.
Mortality in the Americas - PAHO

<table>
<thead>
<tr>
<th>Causas principales</th>
<th>Número de defunciones</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes mellitus</td>
<td>21,26%</td>
</tr>
<tr>
<td>Enfermedades cerebrovasculares</td>
<td>18,11%</td>
</tr>
<tr>
<td>Enfermedades isquémicas del corazón</td>
<td>14,44%</td>
</tr>
<tr>
<td>Enfermedades hipertensivas</td>
<td>8,80%</td>
</tr>
<tr>
<td>Cirrosis y otras enfermedades del hígado</td>
<td>8,31%</td>
</tr>
<tr>
<td>Enfermedades crónicas de las vías respiratorias inferiores</td>
<td>8,11%</td>
</tr>
<tr>
<td>Influenza y neumonía</td>
<td>6,13%</td>
</tr>
<tr>
<td>Enfermedad por virus de la inmunodeficiencia humana (VIH)</td>
<td>5,49%</td>
</tr>
<tr>
<td>Agresiones homicidios</td>
<td>5,03%</td>
</tr>
<tr>
<td>Enfermedades del sistema urinario</td>
<td>4,32%</td>
</tr>
</tbody>
</table>

http://www.paho.org
Estimated worldwide numbers of HIV/HCV co-infected individuals

- HIV 33 million
- HCV 130–180 million
- HIV/HCV co-infection up to 10 million

Outbreaks in IDU & MSM

Global prevalence of HIV/HCV co-infection

Burden of co-infection with HIV and HCV by region, 2013

2.8 million (IQR: 1.6–5.9 million)

HCV: Natural History

- Normal Liver
- Chronic Hepatitis
- Cirrhosis
- HCC ESLD

- HCV Infection: 75-85%
- 20-30%
- 2-7% per year

10 to > 30 years
Progression of Liver Fibrosis Is Common in HIV Patients With HCV Coinfection

• A prospective cohort study assessed the incidence of liver fibrosis progression in coinfected patients (N=282)

• On initial biopsy, 14% of patients had ≥ Metavir stage 2 fibrosis

• After a median follow-up 2.5 years:

  Fibrosis progression 34%

  Increase ≥2 Metavir stages 9%

Fibrosis

Cirrhosis

Hepatitis B Virus (HBV)

Hepatitis C Virus (HCV)

- Higher HBV and HCV chronicity rate
- Increased viral replication
- Decreased HCV-specific immune response

Human Immunodeficiency Virus (HIV)

- Direct effect on stellate cells
- Immune dysregulation
- Cytokine alteration
- Hepatocyte apoptosis

HAART

Liver

Fibrosis

Cirrhosis

Hepatocellular Carcinoma (HCC)

LPS

CD4 Depletion gut mucosa

Adapted from Ingiliz P, Rockstroh JK, Current Opinion in HIV and AIDS 2015
Pathogenesis of HCV-related Liver Disease in HIV Patients With HCV Coinfection

- HIV accelerates the progression of hepatic fibrosis via several T-cell independent mechanisms:

1. **Upregulation of HCV replication**
   - via signalling through CXCR4 and CCR5 co-receptors on hepatocytes

2. **Enhanced fibrogenesis**
   - via augmentation of HCV-related increases in TGF-β1

3. **NF-κB activation**
   - via generation of reactive oxygen species

4. **Independent induction of hepatocyte apoptosis**

5. **Microbial translocation in the gut**
   - via TLR-4 on hepatocytes and stellate cells

CCR4 = chemokine (C-C motif) receptor 5; CXCR4 = chemokine (C-X-C motif) receptor 4; NF-κB = nuclear factor kappa B; TGF-β1 = transforming growth factor beta 1; TLR-4 = toll-like receptor 4.

HIV/HCV co-infection burden: Accelerated disease progression and morbidity

- **↑ Prevalence, especially in some populations**\(^1–^3\)

- **Compared with HCV mono-infected patients, patients co-infected with HIV display:**
  - **↑ viraemia (2–8-fold greater)**\(^1,^4\)
    - **↑ infectivity increases risk of transmission from mother to child (20% vs 6%) and risk of sexual transmission (3% vs <1%)**\(^1,^5\)
  - **↓ likelihood of spontaneously clearing HCV**\(^1,^4\)
  - **↑ hepatic fibrosis (2–5-fold greater), cirrhosis, decompensation, hepatocellular carcinoma and liver-related mortality**\(^1,^5\)

---

Impact of HIV RNA, CD4, or Both on Liver Fibrosis Progression Rate

Time to cirrhosis estimated using liver fibrosis progression rate based on Ishak Fibrosis units/year.

Impact of ART on Overall Liver Mortality in HIV/HCV-Coinfected Patients

- Bonn cohort (1990-2002)
  - 285 HIV/HCV coinfected patients
- Liver-related mortality rates per 100 person-years
  - HAART: 0.45
  - ART: 0.69
  - No therapy: 1.70
- Predictors for liver-related mortality
  - No HAART
  - Low CD4 cell count
  - Increasing age

What is the optimal treatment strategy in HIV/HCV co-infected patients?

- Treat HCV first?
- Treat HIV first?
- Treat HIV/HCV simultaneously?
HIV Suppression Is Associated with Less Hepatic Necroinflammatory Activity

Mehta SH et al. *Hepatology* 2005
Liver Toxicity due to HAART

- 14-20% of patients will develop elevated liver enzymes.
- 2-10% of patients will need to interrupt HAART due to severe liver injury.
- Risk factors:
  - Viral hepatitis B or C
  - First regimen
  - Nevirapine
  - Full dose ritonavir
  - Female sex

Avoid mitochondrial toxicity

J Infect Dis 2002; 186:23-31
## ARVs and Liver Disease

<table>
<thead>
<tr>
<th>ART Drug Class</th>
<th>Liver Toxicity</th>
</tr>
</thead>
</table>
| **NRTI**       | ▪ Reported with most NRTIs  
▪ Steatosis most common with ZDV, d4T, or ddI  
▪ ddI: Prolonged exposure linked to noncirrhotic portal HTN, esophageal varices  
▪ Flares: HIV/HBV-coinfected pts may develop severe hepatic flares when TDF, 3TC, and FTC are withdrawn or when HBV resistance develops  
▪ Dose adjust ABC |
| **NNRTI**      | ▪ NVP > other NNRTIs  
▪ NVP: Severe hepatotoxicity associated with skin rash or hypersensitivity. Risk greater for women with pre-NVP CD4+ cell count > 250 cells/mm³ and men with pre-NVP CD4+ cell count > 400 cells/mm³. NVP in pts with hepatic insufficiency (CP B or C)  
▪ Use EFV with caution in liver disease |
| **PI**         | ▪ All PIs: Drug-induced hepatitis and hepatic decompensation have been reported; greatest frequency with TPV/RTV  
▪ TPV/RTV contraindicated in CP B or C; DRV contraindicated in CP C  
▪ Dose adjust ATV, FPV, IDV  
▪ No boosting in CP B or C |
| **INSTI**      | ▪ DTG/3TC/ABC associated with severe acute exacerbations of hepatitis, which are primarily described in HBV-coinfected pts  
▪ DTG and EVG not recommended in CP C |
Antiretroviral therapy reduces the rate of hepatic decompensation among HIV- and hepatitis C virus-coinfected veterans

Objective:

- To evaluate 10,090 HIV/HCV-co-infected males from the Veterans Aging Cohort Study Virtual Cohort, who had not initiated ART at entry, for incident hepatic decompensation between 1996 and 2010

Results:

- Initiation of ART significantly reduced the rate of hepatic decompensation by 28–41% on average

HCV Disease Progression Remains Faster in Coinfected Patients, Despite Effective ART

If HIV RNA <1000 copies/mL: +65% excess risk
If HIV RNA >1000 copies/mL: +82% excess risk

If CD4 < 200/mm²: +203% excess risk
If CD4 > 200/mm²: 56–63% excess risk

ART, antiretroviral therapy; HCV, hepatitis C virus; HIV, human immunodeficiency virus.

New Era of HCV Therapy

- Discovery of HCV
- FDA approves IFN as the first therapy
- FDA approves RBV to combine with IFN

SVR Rate (%)

- IFN 24 wks: 6%
- IFN 48 wks: 16%
- IFN +RBV 24 wks: 34%
- IFN +RBV 48 wks: 42%
- PEG 48 wks: 39%
- PEG +RBV 48 wks: 54% 56%
- PI +PEG +RBV 24-48 wks: 68%-75%
- SMV +PEG +RBV 24-48 wks: 80%-81%
- SOF +PEG +RBV 12 wks: 89%
- OBV/PTV/RTV 8-12 wks: 90%-99%
- LDV/SOF ±RBV 12 wks: 94%-99%
- ?

Years are not to scale
HCV life cycle

**Cyclophilin A inhibitor**
- Inhibition of cyclophilin A reduces HCV replication

**NS3 inhibitor**
- Inhibits activity of NS3 protease
- Prevents processing of HCV proteins required for replication

**NS5B inhibitor(s)**
- Inhibits NS5B RNA replicase
- Prevents replication of viral genome

**NS5A inhibitor**
- Inhibits activity of NS5A, a multifunctional protein
- Prevents viral replication

**PEG-IFN lambda**
- Type III pegylated interferon
- Expression of receptor is more limited than Alfa, should lead to improved tolerability and safety

Benefits of SVR

Cure!

Reduced Transmission $^{[1]}$

↓ Chirrosis
↓ Descompensation
↓ HCC
↓ Transplant

Clinical improvement $^{[1,2]}$

↓ Mortality
↓ Neoplasias
↓ Diabetes
↓ CVD
↓ Renal
↓ Neurocognitive
↓ QoL improvement

Hepatic

Extrahepatic

Las Opciones de Tratamiento con AAD

Región Estructural

Proteasa

Región No-Estructural

Polimerasa

Viral RNA

Lumen del RE

NS2

NS3

NS5A

NS4A

Inhibidores de Proteasa

“PREVIRs”

Simeprevir
Asunaprevir
Paritaprevir
Grazoprevir

NS5A

Inhibidores de NS5A

“ASVIRs”

Daclatasvir
Ledipasvir
Ombitasvir

NS5B

Inhibidores de Polimerasa

“BUVIRs”

Sofosbuvir
Dasabuvir

Velpatasvir
Elbasvir
Current HCV therapies

**Protease (NS3/4a)**
- Telaprevir
- Boceprevir
- Simeprevir
- Paritaprevir
- Grazoprevir

**NS5a (assembly complex)**
- Daclatasvir
- Ledipasvir
- Ombitasvir
- Elbasvir
- Velpatasvir

**NS5b (RNA-polymerase)**
- Sofosbuvir
- Sofosbuvir
- Sofosbuvir
- Dasabuvir*
- Sofosbuvir

* non-nucleoside RNA polymerase inhibitor
## Current All-Oral Regimens for HCV Infection

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Component Classes</th>
<th>Approved Genotypes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grazoprevir/elbasvir</td>
<td>Protease inhibitor + NS5A inhibitor</td>
<td>1, 4</td>
</tr>
<tr>
<td>Ombitasvir/paritaprevir/ritonavir</td>
<td>Protease inhibitor + NS5A inhibitor</td>
<td>4</td>
</tr>
<tr>
<td>Ombitasvir/paritaprevir/ritonavir + dasabuvir</td>
<td>Protease inhibitor + NS5A inhibitor + polymerase inhibitor</td>
<td>1</td>
</tr>
<tr>
<td>Sofosbuvir + daclatasvir</td>
<td>Nucleotide polymerase inhibitor + NS5A inhibitor</td>
<td>1, 3</td>
</tr>
<tr>
<td>Sofosbuvir/ledipasvir</td>
<td>Nucleotide polymerase inhibitor + NS5A inhibitor</td>
<td>1, 4, 5, 6</td>
</tr>
<tr>
<td>Simeprevir + sofosbuvir</td>
<td>Nucleotide polymerase inhibitor + protease inhibitor</td>
<td>1</td>
</tr>
<tr>
<td>Sofosbuvir/velpatasvir</td>
<td>Nucleotide polymerase inhibitor + NS5A inhibitor</td>
<td>1, 2, 3, 4, 5, 6</td>
</tr>
</tbody>
</table>

References in slidenotes.
AASLD Guidance: HCV/HIV Coinfection

- All pts with HCV should be treated
  - Pts with cirrhosis among highest priority for treatment
  - HCV/HIV coinfection among high priority for treatment
- Even in this era of potent HIV antiretrovirals, pts with HCV/HIV coinfection are at greater risk for rapidly progressive fibrosis and cirrhosis
- “HIV ARV therapy is not a substitute for HCV treatment”
Summary of DDIs Between HCV and HIV Therapies

<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>ATV + RTV</td>
<td>X</td>
<td>∼</td>
<td>∼</td>
<td>√</td>
<td>X</td>
</tr>
<tr>
<td>DRV + RTV</td>
<td>X</td>
<td>∼</td>
<td>√</td>
<td>≈[5]</td>
<td>X</td>
</tr>
<tr>
<td>Tipranavir + RTV</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>EFV or ETR</td>
<td>X</td>
<td>√</td>
<td>≈</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>RPV</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>X</td>
<td>√</td>
</tr>
<tr>
<td>DTG or RAL</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>√</td>
</tr>
<tr>
<td>EVG + COBI</td>
<td>X</td>
<td>∼</td>
<td>√</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>3TC/ABC</td>
<td>√</td>
<td>√</td>
<td>√[4]</td>
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<td>√[3]</td>
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<td>√*</td>
<td>√[2]</td>
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<tr>
<td>TDF</td>
<td>√</td>
<td>∼</td>
<td>√</td>
<td>√</td>
<td>√</td>
</tr>
</tbody>
</table>

*No data.

- No clinically significant interaction expected
- Potential interaction may require adjustment to dosage, timing of administration, or monitoring
- Do not coadminister


Slide credit: clinicaloptions.com
Recommendations for LDV/SOF Use in HCV/HIV Coinfection

**LDV/SOF**

- Can be used with most ARVs
- Avoid use with TDF in pts with CrCl < 60 mL/min
- Avoid use with TDF + RTV or COBI (pending more data)
- For pts receiving RTV- or COBI-containing ART, TAF may be an alternative to TDF during LDV/SOF therapy
- **SOF-based regimens should NOT be used with TPV**
- For combinations anticipated to increase TFV levels, perform baseline and ongoing monitoring for nephrotoxicity
Recommendations for DCV + SOF Use in HCV/HIV Coinfection

- Dose adjustment needed for DCV when used with ATV/RTV, EFV, or ETR, but DCV + SOF not coformulated, allowing adjustment of DCV dose

<table>
<thead>
<tr>
<th>DCV + SOF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decrease DCV dose to 30 mg daily with RTV-boosted ATV</td>
</tr>
<tr>
<td>Increase DCV dose to 90 mg daily with EFV or ETR</td>
</tr>
<tr>
<td><strong>SOF-based regimens should NOT be used with TPV</strong></td>
</tr>
</tbody>
</table>
Recommendations for OBV/PTV/RTV + DSV Use in HCV/HIV Coinfection

- Phase II study of OBV/PTV/RTV + DSV + RBV in HCV/HIV coinfection included pts with ATV- or RAL-based ART only[1]

<table>
<thead>
<tr>
<th>OBV/PTV/RTV + DSV[2]</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ARVs without substantial interactions:</strong> 3TC, ATV, DTG, ENF, FTC, RAL, and TDF</td>
</tr>
<tr>
<td><strong>Should NOT be used with:</strong> DRV, EFV, RTV-boosted LPV, RTV-boosted TPV, ETR, NVP, COBI, or RPV</td>
</tr>
<tr>
<td><strong>If using with other RTV-boosted HIV PI, RTV dose may need to be adjusted (or held) during OBV/PTV/RTV + DSV coadministration; HIV PI should be administered at the same time as the fixed-dose HCV combination</strong></td>
</tr>
<tr>
<td><strong>Should NOT be used in HCV/HIV-coinfected individuals who are not on ART</strong></td>
</tr>
</tbody>
</table>

## Recommendations for SOF/VEL Use in HCV/HIV Coinfection

<table>
<thead>
<tr>
<th>SOF/VEL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Can be used with most ARVs, but <strong>should NOT</strong> be used with EFV, ETR, or NVP</td>
</tr>
<tr>
<td>Avoid use with TDF in pts with CrCl &lt; 60 mL/min</td>
</tr>
<tr>
<td>In pts with CrCl &gt; 60 mL/min, coadministration of VEL and TDF with RTV or COBI did not lead to renal toxicity in 56 pts; renal monitoring is recommended</td>
</tr>
<tr>
<td>For pts receiving RTV- or COBI-containing ART, TAF may be an alternative to TDF during SOF/VEL therapy</td>
</tr>
<tr>
<td><strong>SOF-based regimens should NOT be used with TPV</strong></td>
</tr>
<tr>
<td>For combinations anticipated to increase TFV levels, perform baseline and ongoing monitoring for nephrotoxicity</td>
</tr>
</tbody>
</table>
Ledipasvir/sofosbuvir for 12 Weeks in Patients Coinfected with HCV and HIV-1: ION-4

Study Design:
GT1 and 4 with HIV/HCV co-infection*

Efficacy Results:
GT1 and 4 with HIV/HCV co-infection

<table>
<thead>
<tr>
<th></th>
<th>Overall</th>
<th>Naïve</th>
<th>Exp</th>
<th>No cirrhosis</th>
<th>Cirrhosis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>n</strong>/<strong>N</strong></td>
<td>321/335</td>
<td>142/150</td>
<td>179/185</td>
<td>258/268</td>
<td>63/67</td>
</tr>
<tr>
<td><strong>SVR12 (%)</strong></td>
<td>96</td>
<td>95</td>
<td>97</td>
<td>96</td>
<td>94</td>
</tr>
</tbody>
</table>

ALLY-2: DCV+SOF in HIV/HCV Coinfection

**Primary Endpoint**

<table>
<thead>
<tr>
<th></th>
<th>GT 1</th>
<th>All Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>12-Week Naive</td>
<td>96</td>
<td>97</td>
</tr>
<tr>
<td>12-Week Experienced</td>
<td>98</td>
<td>98</td>
</tr>
<tr>
<td>8-Week Naive</td>
<td>76</td>
<td>76</td>
</tr>
</tbody>
</table>

**SVR12, %**

- 12-Week Naive: 80/83
- 12-Week Experienced: 43/44
- 8-Week Naive: 31/41
- 12-Week Naive: 98/101
- 12-Week Experienced: 51/52
- 8-Week Naive: 38/50

C-EDGE Coinfection: Grazoprevir/Elbasvir for 12 Wks in HIV/HCV Coinfection

- **N = 218 HCV treatment-naive pts; 66% genotype 1a HCV, 60% had HCV RNA > 800,000 IU/mL, 16% cirrhotic**
  - New NS3, NS5A RAVs detected at failure in 4 of 5 pts who relapsed
- **No pt discontinued for AEs and no serious treatment-related AEs**

<table>
<thead>
<tr>
<th></th>
<th>All Pts</th>
<th>GT1a</th>
<th>GT1</th>
<th>GT4</th>
</tr>
</thead>
<tbody>
<tr>
<td>SVR12 (%)</td>
<td>96.3</td>
<td>96.5</td>
<td>95.5</td>
<td>96.4</td>
</tr>
<tr>
<td>n/N =</td>
<td>210/218</td>
<td>139</td>
<td>42</td>
<td>27</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>All Pts</th>
<th>GT1a</th>
<th>GT1</th>
<th>GT4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Discontinued*</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
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<tr>
<td>Relapse</td>
<td>5</td>
<td>4</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Reinfection</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

*Unrelated to virologic failure.

岩查霍 JK, et al. 兰肯 HIV. 2015;2:e319-e327
ASTRAL-5: Sofosbuvir/Velpatasvir for 12 Wks in HIV/HCV Coinfection

- N = 106 pts; HCV treatment experienced: 29%, compensated cirrhosis: 18%, BL NS5A RAVs: 12%
  - Of 2 relapses, 1 treatment experienced, neither with cirrhosis or BL NS5A RAVS
- No significant effect on CrCl regardless of TDF use with or without boosted ARV

HIV-HCV Coinfection study: TURQUOISE-I: 3 DAAs + RBV

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>12-Week Group (n = 31)</th>
<th>24-Week Group (n = 32)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male, n (%)</td>
<td>20 (64.5)</td>
<td>20 (62.9)</td>
</tr>
<tr>
<td>Race, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>24 (77.4)</td>
<td>24 (75.0)</td>
</tr>
<tr>
<td>Black</td>
<td>7 (22.6)</td>
<td>8 (25.0)</td>
</tr>
<tr>
<td>Age, y (mean ± SD)</td>
<td>50.9 ± 6.0</td>
<td>50.9 ± 6.3</td>
</tr>
<tr>
<td>BMI, kg/m² (mean ± SD)</td>
<td>26.4 ± 3.9</td>
<td>27.2 ± 4.3</td>
</tr>
<tr>
<td>HCV RNA level, log₁₀ IU/mL (mean ± SD)</td>
<td>6.54 ± 0.57</td>
<td>6.6 ± 0.78</td>
</tr>
<tr>
<td>CD4+ T-cell count/mm³ (mean ± SD)</td>
<td>633 ± 236</td>
<td>625 ± 296</td>
</tr>
<tr>
<td>IL28B genotype, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CC</td>
<td>5 (16.1)</td>
<td>7 (21.9)</td>
</tr>
<tr>
<td>Non-CC</td>
<td>25 (83.9)</td>
<td>24 (78.1)</td>
</tr>
<tr>
<td>HCV GT/subtype, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1a</td>
<td>27 (87.1)</td>
<td>29 (90.6)</td>
</tr>
<tr>
<td>1b</td>
<td>4 (12.9)</td>
<td>3 (9.4)</td>
</tr>
<tr>
<td>Cirrhosis present, n (%)</td>
<td>6 (19.4)</td>
<td>6 (18.8)</td>
</tr>
<tr>
<td>Prior HCV treatment history</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment-naïve, n (%)</td>
<td>20 (64.5)</td>
<td>22 (68.8)</td>
</tr>
<tr>
<td>Treatment-experienced</td>
<td>11 (35.5)</td>
<td>10 (31.2)</td>
</tr>
<tr>
<td>Prior pegIFN/RBV response, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Relaprair</td>
<td>1 (3.2)</td>
<td>3 (9.4)</td>
</tr>
<tr>
<td>Partial responder</td>
<td>5 (16.1)</td>
<td>2 (6.3)</td>
</tr>
<tr>
<td>Null responder</td>
<td>5 (16.1)</td>
<td>5 (15.6)</td>
</tr>
<tr>
<td>HIV-1 ART regimen, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atazanavir</td>
<td>16 (51.8)</td>
<td>12 (37.5)</td>
</tr>
<tr>
<td>Raltegravir</td>
<td>15 (48.4)</td>
<td>20 (62.5)</td>
</tr>
</tbody>
</table>

3D, co-formulated ART-400/ledipasvir (150/100/25 mg) administered once daily; dasabuvir 250 mg administered twice daily. RBV, ribavirin; weight-based dosing (1000 or 1200 mg), administered twice daily. SVR12, sustained virologic response 12 weeks after the last dose of study drug.

EOTR, end of treatment response; RBV, ribavirin; RVR, rapid virologic response (week 4); SVR4, sustained virologic response at 4 weeks after the end of treatment; SVR12, sustained virologic response at 12 weeks after the end of treatment.
<table>
<thead>
<tr>
<th>Feature</th>
</tr>
</thead>
<tbody>
<tr>
<td>✔ Pangenotypic Efficacy</td>
</tr>
<tr>
<td>✔ Short duration regimens</td>
</tr>
<tr>
<td>✔ No ribavirin required</td>
</tr>
<tr>
<td>✔ Efficacious in patients failing DAAs</td>
</tr>
<tr>
<td>✔ Active in genotype 3</td>
</tr>
<tr>
<td>✔ Without drug interactions</td>
</tr>
<tr>
<td>✔ No limitations in renal insufficiency</td>
</tr>
<tr>
<td>✔ Affordable cost</td>
</tr>
</tbody>
</table>
Hepatitis C Is an INFECTIOUS Virus: Treatment as Prevention


Slide credit: clinicaloptions.com
Treatment Can Prevent Onward Transmission

- Observed and modeled HCV chronic prevalence among PWID in Melbourne, Australia.

![Graph showing HCV chronic prevalence among PWID in Melbourne, Australia over years from 2002 to 2027.](clinicaloptions.com)
The promise of treatment as prevention for hepatitis C: Meeting the needs of people who inject drugs

Magdalena Harris a,*, Eliot Albers b, Tracy Swan c

We argue that HCV treatment as a prevention strategy can only be realisable in a context of enhanced harm reduction access, meaningful community engagement, and enabling environment interventions informed by the needs and perspectives of PWID.

Elimination of Hepatitis C Virus Infection Among People Who Inject Drugs Through Treatment as Prevention: Feasibility and Future Requirements

Jason Grebely,1 Gail V. Matthews,1 Andrew R. Lloyd,2 and Gregory J. Dore1

Table 1. Key Components That Will be Required for the Feasibility of Hepatitis C Virus Treatment as Prevention

<table>
<thead>
<tr>
<th>POPULATION LEVEL</th>
<th>INDIVIDUAL LEVEL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk of HCV transmission</td>
<td>Optimal targeting of HCV treatment among PWID</td>
</tr>
<tr>
<td>???</td>
<td>15</td>
</tr>
</tbody>
</table>

High rates of screening and diagnosis among people who inject drugs (PWID) and linkage to clinical care
Infrastructure for provision of clinical services to PWID, including hepatitis C virus (HCV) treatment
Willingness of PWID to undertake HCV treatment
Therapeutic regimens that optimize treatment adherence and completion
Harm reduction strategies to reduce pretreatment prevalence and prevent reinfection
Cost-effective regimens and public health investment in care for PWID
Global Call for HCV Elimination

- Vision: “A world where viral hepatitis transmission is stopped and everyone has access to safe, affordable, and effective treatment and care”
  - 2020 target: 3 million HCV infections treated
- **Feasible** by scaling up **6 key interventions** to high coverage:
  - Hepatitis B vaccination (including birth dose)
  - Safe injection practices and safe blood
  - Harm reduction for injecting drug users
  - Safer sex (including condom promotion)
  - Hepatitis B treatment
  - Hepatitis C cure

2030 Targets
- 90% Diagnosed
- 80% Treated
- 65% Reduced Mortality

Chronic hepatitis C and HIV: Conclusions

- HIV infected individuals with HCV coinfection remain at higher risk for fibrosis progression and hepatic decompensation
- Therefore HCV therapy is prioritized in most guidelines in this patient group
- The short- and mid-term effects of ART on the progression of HCV-related liver disease largely outweigh the potential risks for long-term toxicity
- Consider drug interactions
- HCV therapy as a case of TasP?
- Safe and even better options are just around the corner
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