Treating Hepatitis C in the Co-infected Patient

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HIV/HCV Coinfection

HIV-infected
- 1 million people have HIV
- Incidence: 40,000/yr
- 15,000 deaths/year
- ~45% are HCV-infected

HCV-infected
- 4 million people have HCV
- Incidence: 40,000/yr
- 8000-10,000 deaths/year
- ~10% are HIV-infected

HIV/HCV Coinfection

HIV Exposure


Impact of HIV on HCV-related Liver Disease Progression

Effect of HIV/HCV Coinfection on Fibrosis Progression Rates


HCV Disease Progression

No Fibrosis

Stage 1: Fibrous expansion of some portal areas

Stage 2: Fibrous expansion of most portal areas with occasional portal to portal bridging

Stage 4: Fibrous expansion of portal areas with marked bridging (portal to portal and portal to central)

Stage 5,6: Cirrhosis, probable or defined

Cirrhotic liver: Gross anatomy of cadaver

Courtesy of Gregory Everson, MD
Liver Disease Staging Needed to Determine if “Watch and Wait” Is Appropriate

- Liver biopsy remains the gold standard
- Non-invasive serum tests
  - Accuracy is reasonable in the “minimal disease range”
- Transient elastography
  - Used extensively in Europe and other regions
  - Not approved for clinical use in the United States but approval is anticipated (2013)

Liver-Related Death Top Cause of Non-AIDS Deaths – 1999-2008

N=33,308; 180,176 person-years; HBsAg+ = 11.5%; HCV+ = 15.3%

Impact of HCV on HIV Disease Progression

- Prospective cohort study of 3111 patients on HAART between 6/96 to 5/99
- 37% were HCV+
- HIV-related progression and death higher in active IVDU with HCV infection
- HCV associated with blunted CD4 recovery
- Deaths from liver disease 3-fold higher


HIV/HCV Co-infection

- In 2005, the FDA approved peginterferon alfa-2a and ribavirin as treatment for HCV disease in HCV/HIV coinfection
Virologic Response: PegIFN Alfa-2b + RBV


ACTG 5071 Study: SVR

**APRICOT Study: SVR**

- PegIFN alfa-2a 180 µg QW + RBV 800 mg/d: 40 (n = 289)
- PegIFN alfa-2a 180 µg QW + Placebo: 20 (n = 286)
- IFN alfa-2a 3 MIU TIW + RBV 800 mg/d: 12 (n = 285)


**Case Study**

- 61-year-old European-American man with long-standing HIV disease, hyperlipidemia and chronic HCV infection
  - Liver biopsy reveals cirrhosis
  - No clinical signs – no ascites, encephalopathy, bleeding or lower extremity edema
- CT scan of his liver: nodular appearance without mass
- Upper endoscopy: no significant varices
- Additional laboratory tests
  - Platelet count = 125,000/mm³
  - Total bilirubin = 1.0
  - INR = 1.2
  - Serum Cr = 0.9
    - MELD score = 8
He initiates treatment with peginterferon alfa (PegIFN) + ribavirin (RBV)
- RBV dose selected is 400 mg BID
- Baseline HCV RNA is 2.45 million IU/mL; genotype 1b
- HIV disease is well controlled with darunavir/ritonavir + TDF + FTC

Is this the correct dose of RBV?
What is the likelihood of SVR?
Is there a role for IL28B testing?

PARADIGM: Weight-based RBV in HIV/HCV Coinfection

Double-blinded, phase IV, 1:2 randomization (N=410)

- PegIFN alfa-2a (40 KD) 180 µg/week (N=135)
- Plus RBV 800 mg/day
- PegIFN alfa-2a (40 KD) 180 µg/week (N=275)
- Plus RBV 1,000/1,200 mg

Follow up

Study weeks

0 12 24 48 72

Case Study (Continued)

- He tolerates PegIFN + RBV reasonably well
  - Anemia at treatment week 6, which is managed with epoetin alfa 40,000 IU SC weekly
- HCV RNA decline at treatment week 4 is ~1.3 \( \log_{10} \) and at treatment week 12 ~2.5 \( \log_{10} \)
- However, at treatment week 24, his HCV RNA is detectable at 80,890 IU/mL
  - Treatment is discontinued
- What is the role of HCV PIs – telaprevir and boceprevir in HIV/HCV coinfected patients?
EACS Guideline Recommendations for Use of PegIFN in HCV/HIV-Coinfected Pts

Two Protease Inhibitors Approved for Genotype 1 HCV Infection

<table>
<thead>
<tr>
<th>Protease Inhibitor</th>
<th>Additional Regimen Components</th>
<th>Considerations</th>
</tr>
</thead>
</table>
| Boceprevir 800 mg TID (q7-9hrs) | PegIFN alfa + weight-based RBV | • Naive to previous therapy  
• Previous treatment failure  
• Compensated cirrhosis  
• RGT |
| Telaprevir 750 mg TID (q7-9hrs) | PegIFN alfa + weight-based RBV | • Naive to previous therapy  
• Previous treatment failure  
• Compensated cirrhosis  
• RGT |

- For patients with genotype 2/3 infection, HCV therapy with PegIFN + RBV remains the standard of care

SPRINT 2: Influence of Race on SVR with PegIFN + RBV ± Boceprevir

<table>
<thead>
<tr>
<th>Race</th>
<th>White</th>
<th>Black</th>
</tr>
</thead>
<tbody>
<tr>
<td>PR + BOC</td>
<td>68</td>
<td>53</td>
</tr>
<tr>
<td>PR + BOC RGT</td>
<td>67</td>
<td>41</td>
</tr>
<tr>
<td>PR</td>
<td>40</td>
<td>23</td>
</tr>
</tbody>
</table>

Efficacy

Safety + tolerability

Drug-drug interactions

Adherence
- Pill burden of HCV therapy + ARV therapy
### Phase 2 Studies of HCV PI + PR

<table>
<thead>
<tr>
<th></th>
<th>Telaprevir</th>
<th>Boceprevir</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Number of patients</strong></td>
<td>TVR, 38; Control, 22</td>
<td>BOC, 64; Control, 34</td>
</tr>
<tr>
<td><strong>HCV population</strong></td>
<td>Naïve, genotype 1</td>
<td>Naïve, genotype 1</td>
</tr>
<tr>
<td><strong>HIV population</strong></td>
<td>CD4 ≥500; HIV ≤100,000 c/mL</td>
<td>CD4 ≥ 200 cells/mm³</td>
</tr>
<tr>
<td></td>
<td>CD4 ≥ 300; HIV ≤50 c/mL</td>
<td>HIV RNA ≤50 c/mL</td>
</tr>
<tr>
<td><strong>Antiretroviral therapy</strong></td>
<td>None (n=7) or EFV (n=16) or</td>
<td>No NNRTIs</td>
</tr>
<tr>
<td></td>
<td>ATV/r (n=15) + TDF/FTC</td>
<td>ATV/r (n=20); DVR/r (n=16);</td>
</tr>
<tr>
<td></td>
<td></td>
<td>DRV/r (n=12); RAL (n=11)</td>
</tr>
<tr>
<td><strong>HCV regimen</strong></td>
<td>TLY 750 mg Q8H or 1125 mg Q8H (if EFV co-admin) + pegIFN-2a + RBV 800 mg/day</td>
<td>BOC 800 mg Q8H + pegIFN-2b + weight based RBV (600–1400 mg/day)</td>
</tr>
<tr>
<td><strong>Lead-in</strong></td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Duration of PI</strong></td>
<td>12 weeks</td>
<td>44 weeks</td>
</tr>
<tr>
<td><strong>Duration of PR</strong></td>
<td>48 weeks</td>
<td>48 weeks</td>
</tr>
<tr>
<td><strong>Virologic futility rules</strong></td>
<td>Week-4 or 8 or 12 HCV RNA &gt;1,000 IU/mL</td>
<td>Week-12 &lt;2 log₁₀ decline</td>
</tr>
<tr>
<td></td>
<td>Week-24 Detectable HCV RNA</td>
<td>Week-24 Detectable HCV RNA</td>
</tr>
<tr>
<td><strong>HCV PI PK measured</strong></td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>ART PK measured</strong></td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

### Study 110: Telaprevir in HIV/HCV Co-infected Patients

**Part A:** no ART

- **T/PR**: Telaprevir + Pegylated interferon/ribavirin, Follow-up
- **PR 48 (control)**: Placebo + Pegylated interferon/ribavirin, Follow-up

**Part B:** ART (EFV/TDF/FTC or ATV/r + TDF + FTC or 3TC)

- **T/PR**: Telaprevir + Pegylated interferon/ribavirin, Follow-up
- **PR 48 (control)**: Placebo + Pegylated interferon/ribavirin, Follow-up

PR – Pegylated interferon/ribavirin, TVR – Telaprevir, SVR – Sustained virologic response

Study 110: SVR Rates 12 Weeks Post-Treatment (SVR12)

Patients with Undetectable HCV RNA (%)

- No ART
- EFV/TDF/FTC
- ATV/r/TDF/FTC
- Total

<table>
<thead>
<tr>
<th>n/N</th>
<th>TVR/PR</th>
<th>PR</th>
</tr>
</thead>
<tbody>
<tr>
<td>5/7</td>
<td>71</td>
<td>33</td>
</tr>
<tr>
<td>11/16</td>
<td>69</td>
<td>50</td>
</tr>
<tr>
<td>12/15</td>
<td>80</td>
<td>50</td>
</tr>
<tr>
<td>28/38</td>
<td>74</td>
<td>45</td>
</tr>
</tbody>
</table>

Futility rules: W12: <2 log_{10} decline; W24: HCV RNA ≥ LLOQ

BL characteristics were well balanced, but cirrhosis: 1-control, 4-BOC

BOC + PegIFN + RBV for HCV/HIV Coinfection (Interim Analysis)

Phase II, BOC-double-blinded 800 mg TID, PEG 2b 1.5 µg/kg QW/RBV WB

- HIV VL <50
- HCV GT1 naïve
- n=100 (2:1)

- Futility rules: W12: <2 log_{10} decline; W24: HCV RNA ≥ LLOQ
- BL characteristics were well balanced, but cirrhosis: 1-control, 4-BOC

Interim Analysis: SVR Rates 12 Weeks Post-Treatment (SVR12)

- Interim efficacy analysis
  - 3 BOC patients had not yet reached SVR12 time point

\[
\begin{array}{c|c|c}
\text{BOC + P/R} & \text{SVR12 (%)} & \text{n/N} \\
\hline
60.7 & 37/61 \\
26.5 & 9/34 \\
\end{array}
\]

*3 patients with missing data achieved SVR4.


Tolerability and Safety: First Signals from Pilot Trials

- 34% and 23% of TVR/PR and PR patients, respectively had rash; no severe rashes were reported in either group
- Preliminary safety data of BOC/PR and TVR/PR in co-infected patients showed a profile consistent with that observed in mono-infected patients (Anemia: BOC 41% vs. 26%; TVR 18% vs. 18%)
- In BOC, HIV breakthroughs were observed in 3/64 patients in the BOC group and 4/34 patients in the control group
- In TVR, no HIV breakthroughs

Boceprevir: Metabolism and Drug-Drug Interactions

- Substrate of aldoketoreductase → primary pathway
- Substrate of CYP3A4/5
  - Coadministration of EFV (CYP3A4/5 inducer) decreased BOC mean exposure 19% to 44% and increased efavirenz mean exposure 11% to 20%
  - No RTV boost
- Strong CYP3A4 inhibitor without evidence of induction
  - BOC → Midazolam AUC markedly increased
- Substrate for the efflux inhibitor P-glycoprotein (P-gp)
- No drug-drug interaction with tenofovir


Boceprevir Exposure Is Decreased by Efavirenz

<table>
<thead>
<tr>
<th>Treatment</th>
<th>LSmean*</th>
<th>Ratio Estimate, % (90% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BOC AUC&lt;sub&gt;0-8h&lt;/sub&gt;, ng•h/mL</td>
<td>BOC: 6,913</td>
<td>81 (75–89)</td>
</tr>
<tr>
<td></td>
<td>BOC + EFV: 5,630</td>
<td></td>
</tr>
<tr>
<td>EFV AUC&lt;sub&gt;0-24h&lt;/sub&gt;, ng•h/mL</td>
<td>EFV: 78,667</td>
<td>120 (115–126)</td>
</tr>
<tr>
<td></td>
<td>EFV + BOC: 94,655</td>
<td></td>
</tr>
</tbody>
</table>

- The clinical outcome of this observed reduction of boceprevir trough concentrations has not been directly assessed

SD, single dose.
*Model-based (least squares) geometric mean, ANOVA extracting the effects due to treatment and volunteer.

Kassera C, et al. CROI 2011. Abst. 118; Boceprevir EU SmPC.
**Effect of ATV/r, LPV/r and DRV/r Coadministration on Boceprevir PK**

<table>
<thead>
<tr>
<th>Coadministered Drug</th>
<th>Ratio Estimate of Coadministered Drug (In Combination vs. Boceprevir Alone)</th>
<th>GMR (90% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>AUC&lt;sub&gt;τ&lt;/sub&gt;</td>
<td>C&lt;sub&gt;max&lt;/sub&gt;</td>
</tr>
<tr>
<td>Atazanavir</td>
<td>0.95 (0.87, 1.05)</td>
<td>0.93 (0.80, 1.08)</td>
</tr>
<tr>
<td>Lopinavir</td>
<td>0.55 (0.49, 0.61)</td>
<td>0.50 (0.45, 0.55)</td>
</tr>
<tr>
<td>Darunavir</td>
<td>0.68 (0.65, 0.72)</td>
<td>0.75 (0.67, 0.85)</td>
</tr>
</tbody>
</table>

- Coadministration with ATV/r does not alter boceprevir AUC<sub>τ</sub>, but coadministration with LPV/r and DRV/r decreases boceprevir AUC<sub>τ</sub> 45% and 32%, respectively.

GMR, geometric least squares mean ratio.

Hulskotte E, et al. CROI 2012. Abst. 771LB.

**Effect of Boceprevir Coadministration on PK of Ritonavir-Boosted ATV, LPV and DRV**

<table>
<thead>
<tr>
<th>Coadministered Drug</th>
<th>Ratio Estimate of Coadministered Drug (In Combination vs. Alone)</th>
<th>GMR (90% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>AUC&lt;sub&gt;0-last&lt;/sub&gt;</td>
<td>C&lt;sub&gt;max&lt;/sub&gt;</td>
</tr>
<tr>
<td>Atazanavir</td>
<td>0.65 (0.55, 0.78)</td>
<td>0.75 (0.64, 0.88)</td>
</tr>
<tr>
<td>Lopinavir</td>
<td>0.66 (0.60, 0.72)</td>
<td>0.70 (0.65, 0.77)</td>
</tr>
<tr>
<td>Darunavir</td>
<td>0.56 (0.51, 0.61)</td>
<td>0.64 (0.58, 0.71)</td>
</tr>
</tbody>
</table>

- Boceprevir coadministration reduces the exposure of ATV, LPV, and DRV by 35%, 34%, and 44%, respectively, and reduces trough concentrations 49%, 43%, and 59%, respectively.

- Mean ATV C<sub>min</sub> decreased from 693 ng/mL to 357 ng/mL; mean LPV C<sub>min</sub> decreased from 6,730 ng/mL to 3,805 ng/mL; mean DRV C<sub>min</sub> decreased from 3,220 ng/mL to 1,321 ng/mL.

GMR, geometric least squares mean ratio.

Hulskotte E, et al. CROI 2012. Abst. 771LB.
### Boceprevir: Drug-Drug Interactions with HIV Antiretrovirals

<table>
<thead>
<tr>
<th>HIV Antiretroviral</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Studies Completed</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Atazanavir/r</strong></td>
<td>• In general, coadministration not recommended</td>
</tr>
<tr>
<td></td>
<td>• EMEA: coadministration may be considered on a case-by-case basis if the patient has no prior HIV drug resistance and is virologically suppressed</td>
</tr>
<tr>
<td><strong>Darunavir/r</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Fosamprenavir/r</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Lopinavir/r</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Efavirenz</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Raltegravir</strong></td>
<td>• No dose adjustment required</td>
</tr>
</tbody>
</table>


### Effect of HIV PIs on Telaprevir

<table>
<thead>
<tr>
<th>HIV Antiretroviral</th>
<th>TVR concentration (ng/mL)</th>
<th>Time (hours)</th>
<th>AUC ↓</th>
</tr>
</thead>
<tbody>
<tr>
<td>LPV</td>
<td>n=14</td>
<td>0 2 4 6 8</td>
<td>54%</td>
</tr>
<tr>
<td>ATV</td>
<td>n=17</td>
<td>0 2 4 6 8</td>
<td>20%</td>
</tr>
<tr>
<td>DRV</td>
<td>n=16</td>
<td>0 2 4 6 8</td>
<td>35%</td>
</tr>
<tr>
<td>fAPV</td>
<td>n=20</td>
<td>0 2 4 6 8</td>
<td>32%</td>
</tr>
</tbody>
</table>

Van Heeswijk. CROI 2011.
Effect of Telaprevir on HIV PIs

APV = amprenavir


Regimen | TVR AUC (90% CI) | ARV AUC (90% CI)
--- | --- | ---
TVR 1125 mg q8h | EFV | ↓18%
 | TDF | ↓18%
TVR 1500 mg q12h | EFV | ↓15%
 | TDF | ↓20%

### Telaprevir: Drug-Drug Interactions With ARVs

<table>
<thead>
<tr>
<th>HIV Antiretroviral</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Studies Completed</strong></td>
<td></td>
</tr>
<tr>
<td>Atazanavir/r</td>
<td>Clinical and laboratory monitoring for hyperbilirubinaemia is recommended</td>
</tr>
<tr>
<td>Darunavir/r</td>
<td></td>
</tr>
<tr>
<td>Fosamprenavir/r</td>
<td>Coadministration not recommended</td>
</tr>
<tr>
<td>Lopinavir/r</td>
<td></td>
</tr>
<tr>
<td>Efavirenz</td>
<td>TVR dose increase necessary (1,125 mg q8h)</td>
</tr>
<tr>
<td>Raltegravir</td>
<td>No dose adjustment required</td>
</tr>
<tr>
<td>Tenofovir</td>
<td>Increased clinical and laboratory monitoring is warranted</td>
</tr>
<tr>
<td><strong>Studies Not Completed</strong></td>
<td></td>
</tr>
<tr>
<td>Etravirine; rilpivirine</td>
<td>Studies planned</td>
</tr>
<tr>
<td>Abacavir; zidovudine</td>
<td>An effect of telaprevir on UDP-glucuronyltransferases cannot be ruled out and may affect plasma concentrations of abacavir or zidovudine (not studied)</td>
</tr>
</tbody>
</table>

UDP, glucuronosyltransferase: uridine 5'-diphospho-glucuronosyltransferase.

Telaprevir EU SmPC.

### Treatment Options for HIV/HCV Genotype 1 Patients: DHHS Guidelines

**Preliminary recommendations on use of boceprevir or telaprevir in HIV/HCV genotype 1 coinfected patients**

<table>
<thead>
<tr>
<th>Patient Group</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients not on ART</td>
<td>Use either boceprevir or telaprevir</td>
</tr>
<tr>
<td>Patients receiving RAL + 2 NRTIs</td>
<td>Use either boceprevir or telaprevir</td>
</tr>
<tr>
<td>Patients receiving ATV/r + 2 NRTIs</td>
<td>Use telaprevir at the standard dose. Do not use boceprevir.</td>
</tr>
<tr>
<td>Patients receiving EFV + 2 NRTIs</td>
<td>Use telaprevir at increased dose of 1,125 mg every 7-9 hours. Do not use boceprevir.</td>
</tr>
</tbody>
</table>

*These recommendations may be modified as new drug interaction and clinical trial information become available.

Case Study (Continued)

- His physician switches his antiretroviral therapy to atazanavir/ritonavir + TDF + FTC
- Patient is treated with peginterferon, ribavirin and telaprevir
  - He achieves HCV eradication
- He is monitored every 6 months with ultrasound for HCC
  - Routine screening reveals a 2 cm solitary liver mass
  - Further evaluation with MRI with contrast highly suggestive of HCC
  - AFP is elevated ~386 ng/dL
- He is referred for liver transplant evaluation
  - Is this an effective strategy?
Management of Newly Diagnosed Gt 1 HCV/HIV–Coinfected Pts

- Patients with newly diagnosed genotype 1 HCV infection
- Perform transient elastography (where available) and/or liver biopsy

F1
- Treatment with peginterferon alfa and ribavirin and an HCV protease inhibitor
- Treatment for 24 weeks if HCV RNA undetectable and RVR
- Treatment if HCV RNA detectable or ETR, high IL-28B CC genotype, severe ETR, or high LDH

F2
- Treatment with peginterferon alfa and ribavirin and an HCV protease inhibitor
- Treatment for 48 weeks if HCV RNA undetectable and RVR
- Treatment if HCV RNA detectable or ETR, high IL-28B CC genotype, severe ETR, or high LDH

F3
- Treatment with peginterferon alfa and ribavirin and an HCV protease inhibitor
- Treatment for 72 weeks if HCV RNA undetectable and RVR
- Treatment if HCV RNA detectable or ETR, high IL-28B CC genotype, severe ETR, or high LDH

F4
- Treatment with peginterferon alfa and ribavirin and an HCV protease inhibitor
- Treatment for 72 weeks if HCV RNA undetectable and RVR
- Treatment if HCV RNA detectable or ETR, high IL-28B CC genotype, severe ETR, or high LDH

*Median fibrosis score: F0 = no fibrosis; F1 = portal fibrosis, no septae; F2 = portal fibrosis, few septae; F3 = bridging fibrosis; F4 = cirrhosis.


Management of Gt 1 HCV/HIV–Coinfected Pts by Fibrosis Stage, Prior Tx Outcome

- Treatment Naive
  - F0/1: Individual decision
  - F2/3: Triple therapy
  - F4: Triple therapy

- Previous Relapser
  - F0/1: Individual decision/triple therapy
  - F2/3: Triple therapy
  - F4: Triple therapy

- Previous Nonresponder
  - F0/1: Defer
  - F2/3: Defer
  - F4: Defer

*Monitor fibrosis stage annually, preferably with 2 established methods. Treat with triple therapy, if rapid progression.

Summary: HIV/HCV Coinfection

- HCV remains a major problem in HIV-infected patients with well-controlled HIV disease
- Current treatment has low efficacy but SVR is strongly linked to better outcomes
- Hepatitis C protease inhibitors in combination with PegIFN + RBV are promising but
  - Drug-drug interactions with ART
  - Limited data on efficacy and safety
- Transplant is an option but remains limited in the United States

HCV Life Cycle and DAA Targets

## Select DAAs in Clinical Development

<table>
<thead>
<tr>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Protease Inhibitors</strong></td>
<td>ABT-450</td>
<td>BMS-650032</td>
</tr>
<tr>
<td></td>
<td>ACH-1625</td>
<td>CTS-1027</td>
</tr>
<tr>
<td></td>
<td>GS 9451</td>
<td>Danoprevir</td>
</tr>
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<td>Mk-5172</td>
<td>GS 9256</td>
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<td>VX-985</td>
<td>IDX320</td>
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<tr>
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<td></td>
<td>Vaniprevir</td>
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<td>Boceprevir</td>
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<td></td>
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<td>Telaprevir</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TMC435</td>
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<tr>
<td><strong>Nonnucleoside polymerase inhibitors</strong></td>
<td>BI 207127</td>
<td>BMS-650032</td>
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<tr>
<td></td>
<td>IDX375</td>
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<tr>
<td><strong>Nucleoside polymerase inhibitors</strong></td>
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## Evolution of HCV Therapy

### 2001

- PegIFN/RBV
Evolution of HCV Therapy

2001 2011

- PegIFN/RBV
- Protease inhibitor

Beyond

- Nucleos(t)ide polymerase inhibitor
- Nonnucleoside polymerase inhibitor
- NS5A inhibitor
Survival After OLT in HCV and HCV/HIV Infected Persons

Survival rates for HCV/HIV patients and HCV patients:
- HCV/HIV patients: 76% (95% CI: 66%-84%) and 60% (95% CI: 47%-71%) for 1 and 3 years, respectively.
- HCV patients: 92% (95% CI: 87%-95%) and 79% (95% CI: 72%-84%) for 1 and 3 years, respectively.

HIV-TR Multicenter Cohort Study

- CD4: ≥100 cells/mm³ prior to transplant; or ≥200 cells/mm³ prior to transplant if there is a history of an OI.
- HIV RNA: If patient is on ARVs, <50 copies/mL.
  - Patients who are unable to tolerate ARV therapy due to exacerbation of underlying liver disease are eligible if the HIV clinician is confident they can predict HIV suppression post-transplant.
- No active substance use.
- Minimal cardiac and pulmonary disease.
- Adequate social support.
- HCV/HIV (n=89) compared to HCV alone (n=235).

Survival According to HIV Status and Risk Assessment

- High risk HIV/HCV: BMI <21 kg/m²; combined liver-kidney transplant or anti-HCV positive donor; poor survival and high incidence of graft loss
- Standard risk HIV/HCV similar to HCV alone