Update: Coinfection with HIV/Hepatitis C
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No disclosures or conflicts of interest

Bank Account: $0.00
Objectives:
• Review epidemiology of HIV/HCV co-infection
• Review risk factors for acute hepatitis C
• Discuss HIV/Hep C specific treatment considerations
• Note future therapies for HCV

Epidemiology
• CDC estimates 1.2 million people in the United States HIV infection
• About 25% of HIV + individuals are also infected with HCV (U.S)
• About 80% of HIV+ injection drug users (IDUs) also have HCV
• Sexual transmission is an increasing risk factor for acute HCV acquisition

Increasing acute hepatitis C in MSM

Mount Sinai, New York City – Case control study 2005-2010

- HIV positive, MSM patients
- 22 case patients with acute HCV infection, 53 matched controls
- Sexual transmission was the most likely mode of transmission of acute HCV
- **Unprotected receptive** anal intercourse with ejaculation and sex while high on **meth**amphetamine were the most important predictors of HCV infection

Sexual transmission of hepatitis C virus among HIV-infected men who have sex with men-New York City, 2005-2010. MMWR 60(28);945-950, 2011.

Impact of HIV/HCV co-infection

- Meta-analysis showed that co-infected patients were 3X more likely to progress to cirrhosis or decompensated liver disease
- Liver-related deaths were on of the highest causes of non-AIDS related deaths in D:A:D study
- HCC “similar” if Hep C w/wo HIV* (2009 meta)


Increased risk of hepatic decompensation and HCC in HIV/HCV-co-infected patients despite ART*

- Retrospective cohort study of 4,286 cART-treated HIV/HCV-coinfected and 6,639 HCV-monoinfected patients in the Veterans Aging Cohort Study Virtual Cohort (1997-2010)
- Male, 2/3 AA, 25% ETOH; HCV tx naïve; cART for at least 1 year
- Hepatic decompensation events and death were evaluated
- Compared to HCV-monoinfected patients, cART-treated HIV/HCV-coinfected had
  - Higher hepatic decompensation (7.1% vs 5.7%, aHR=1.76)
  - Higher hepatocellular carcinoma (1.2% vs 0.9%, aHR=1.69)
- After decompensation, mortality was higher (75.2% vs 56.8%)


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Historical Cure Rates for HIV HCV Genotype 1 treatment

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Percentage of SVR</th>
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</thead>
<tbody>
<tr>
<td>PegIFN+RBV 12m</td>
<td>55</td>
</tr>
<tr>
<td>PegIFN 12m</td>
<td>39</td>
</tr>
<tr>
<td>IFN+RBV 12m</td>
<td>42</td>
</tr>
<tr>
<td>IFN+RBV 6m</td>
<td>34</td>
</tr>
<tr>
<td>IFN 12m</td>
<td>16</td>
</tr>
<tr>
<td>IFN 6m</td>
<td>6</td>
</tr>
</tbody>
</table>

Percentage of SVR

3. Fabrice Carat, MD et al. JAMA. 2004;292:2839-2848
Boceprevir

- Protease inhibitor that binds reversibly to the HCV NS3 active site
- SPRINT-2 (naïve), RESPOND-2 (re-TX)
  - 66% Overall SVR in treatment naïve and treatment experienced genotype 1 patients
  - EXCLUDED HIV+
HIV/HCV Phase 2b trial

- 100 txt-naive HIV/HCV coinfected genotype 1 patients
- Optimized ART, stable HIV viral load (< 50 copies/mL) and CD4 T-cells at least 200
- PR+BOC vs PR

<table>
<thead>
<tr>
<th></th>
<th>CONTROL PR</th>
<th>Boceprevir BOC</th>
<th>Difference %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 4</td>
<td>3/34 (8.8)</td>
<td>3/64 (4.7)</td>
<td>-4.1</td>
</tr>
<tr>
<td>Week 8</td>
<td>5/34 (14.7)</td>
<td>27/64 (42.2)</td>
<td>27.5</td>
</tr>
<tr>
<td>Week 12</td>
<td>8/34 (23.5)</td>
<td>38/64 (59.4)</td>
<td>35.8</td>
</tr>
<tr>
<td>Week 24</td>
<td>11/34 (32.4)</td>
<td>47/64 (73.4)</td>
<td>41.1</td>
</tr>
<tr>
<td>Week 48</td>
<td>10/34 (29.4)</td>
<td>39/61 (63.9)</td>
<td>34.5</td>
</tr>
<tr>
<td>SVR12</td>
<td>9/34 (26.5)</td>
<td>37/61 (60.7)</td>
<td>34.2</td>
</tr>
</tbody>
</table>


BOC + RAL

- Boceprevir did not affect Raltegravir levels
- BPV dose: 800mg TID (200mg)
- Raltegravir is currently the best partner for boceprevir combination therapy in HIV/HCV coinfection

de Kanter C, Blonk M, Colbers A, Fillekes Q, Schouwenberg B, Burger D. The Influence of the HCV Protease Inhibitor Bocepravir on the Pharmacokinetics of the HIV Integrase Inhibitor Raltegravir. 19th Conference on Retroviruses and Opportunistic Infections, March 5-8, 2012; abstract 772LB

Telaprevir

- Protease inhibitor that targets the NS3/4a HCV serine protease
- PROVE, ADVANCE (naïve) REALIZE (re-TX) trials
  - 66% Overall SVR in treatment naïve and treatment experienced genotype 1 patients

McHutchison, JG. Telaprevir with peginterferon and ribavirin for chronic HCV genotype 1 infection. NEJM 2009; 360:1827-38.
Jacobson, IM, et. al. Telaprevir for previously untreated chronic hepatitis C infection. NEJM 2011; 364:2405-16.
HIV/HCV Phase 2b trial

- 60 HIV/HCV genotype 1 coinfected treatment naïve subjects
- Part A: Not on ART received TVR12/PR48
- Part B: On ART (ten/FTC with EITHER efavirenz OR ataz/r) received TVR12/PR48: pharmacokinetic study

Results

- Higher SVR12 rates 74%
- No dose adjustments needed for ATV/r
- Double doses of TVR could be adjusted with EFV
- Telaprevir traditional dose: 750mg TID (375mg)

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CLIFFS NOTES

- Telaprevir: wk 1->12 ;48 PR
  - raltegravir
  - atanazavir/ r
    ( efavirenz →2x telaprevir dose)
- Boceprevir: wk 5->48 w/ PR until 48)
  - Raltegrevir
  - No PIs
- Use cART if possible ( liver decomp rate)
- HCV VL wk 4, (8), 12, 24, end, 3 months post
- D/C Tx: VL >1000 wk 12 TPV; wk 24 BPV if VL+

*monoHCV: ER= Early Response=UD wk 8 & 24, stop ALL tx wk 28
Case 1

- 54 yo M with well-controlled HIV, last CD4 580 on tenofavir/FTC and raltegrevir
- New dx chronic HCV, genotype 1a, HCV Quant 2.4 million
- started on Boceprevir
- Week 2 - Hgb drops from 13.8 to 12.5
- Week 4 - Hgb 11.8, HCV undetectable
- Pt gets started on BOC + PR
- Week 6 – Hgb 9.8

What do you do?

A. Stop all treatment
B. Stop Boceprevir
C. Start erythropoietin
D. Decrease Ribavirin dose
E. Do nothing
Anemia

What do you do?

A. Stop all treatment
B. Stop Boceprevir
C. Start erythropoietin
D. Decrease Ribavirin dose
E. Do nothing
Ribavirin dose reduction

- RCT 500 patients of PR+BOC with Hgb<10
- Randomized to receive RBV dose reduction 200-400mg/d vs 40,000 IU/wk subq epoetin alfa
- No statistical difference in SVR rates
- Similar findings post-hoc analysis for TPV
- Avoid AZT with ribavirin (D4T, DDI)


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Case 2

- 45 yo F with well controlled HIV CD4 445, chronic HCV, genotype 1b
- Started on TPV+PR
- Week 2 labs stable
- Week 4 – presents with mild erythematous macular rash on chest; Given Benadryl and hydrocortisone cream
Week 5 Follow-up

TPV-Associated TEN-SJS
Case 3

- 24 yo M with HIV, well controlled on ten/FTC/efav, CD4 800’s
- Routine labs showed elevated transaminitis, HCV Ab positive, confirmatory HCV quant 679,000
- Dx with acute hepatitis C, genotype 1a
- Follow HCV quant in 8 weeks 240,000

How should you proceed?

A. Start Boceprevir+PR treatment
B. Start Telaprevir+PR treatment
C. Change ARV regimen to Truvada, Isentress first
D. Monitor chronic HCV, do not treat
Side effects/other issues

• Telaprevir (no renal dose)
  – Rash (TEN, DRESS)
  – Erythema multiforme
  – Anemia
  – Neutropenia
  – Thrombocytopenia
  – n/v/d
  – Anal Pruritis (20g FAT)
    • 2 tbspn peanut butter
    • ¾ cup ice cream
  – Increased Uric acid

• Boceprevir (no renal)
  – Anemia
  – Neutropenia
  – Thrombocytopenia
  – Nausea/diarrhea
  – Insomnia
  – Alopecia
  – Rash
  – Arthralgia

Future therapies

• Simeprevir + PR
• Sofosbuvir + RBV +/- PegIFN
• Danoprevir + Mericitabine +/- RBV
• GS-9256 + Tegobuvir +/- RBV +/- PegIFN
• VX-222 + TPV + RBV +/- PegIFN
• Daclatasvir + Asunaprevir +/- PR
Last words

- Continue to screen for HCC in cirrhotic patients
- Continue risk reduction education to prevent HCV re-infection
- Hep A/B vaccination

References

- MMWR. Sexual transmission of hepatitis c virus among HIV-infected men who have sex with men-New York City, 2005-2010. MMWR 60(28);945-950, 2011.
- Poordad, F. Boceprevir for untreated chronic HCV genotype 1 infection. NEJM 2011; 364:1195-1206.