Hepatitis C Virus (HCV) and HIV Co-infection: What’s new and what you need to know

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Main points to take home

• Identify 2 new drugs available for HCV treatment

• Understand drug-drug interactions between studied HIV antiretroviral drugs and HCV protease inhibitors are important

• Understand the importance of HAV and HBV vaccination in chronic HCV
HCV: How common is it in the US?

- Estimated 3.9 million people in the US have HCV infection. Recent figures that include populations at high risk indicate that this number may be as high as 5 to 7 million.
- HCV infection has now surpassed HIV as the leading cause of death among chronic viral diseases in the United States, and HIV/HCV coinfection is associated with an increased risk of cirrhosis and liver failure.
- Because modes of HIV and HCV transmission (through skin blood exposure and sexual intercourse) are shared, 20% to 30% of patients with HIV infection are coinfected with HCV.
What’s the natural history of HCV?

- HCV progresses to chronic disease in 55% to 85% of cases
- Cirrhosis occurs in 20% of HCV only infected patients within 20 years of infection and is the leading cause of liver transplants in the US
- HIV co-infected patients have a > 2x increased risk of cirrhosis than HCV only patients
HCV genotypes: Why do they matter?

• HCV genotype 1 is responsible for 60-70% of infections in the US, but treatment with peginterferon alfa and ribavirin is effective in only 40-50% of patients with HCV genotype 1 only infection

• In HIV-positive patients with genotype 1 HCV infection and a high plasma HCV RNA level (> 800,000 IU/mL), cure (SVR) was achieved in only 20% of patients
May 2011, US Food and Drug Administration (FDA) approved 2 HCV non structural protein 3 protease inhibitors (NS3 PIs), boceprevir and telaprevir to treat chronic HCV genotype 1 infection. Neither drug is currently FDA approved for HIV-HCV co-infection.
Results from the study of telaprevir in HIV/HCV-coinfected patients naive to HCV treatment. Only participants not on ARVs, or on efavirenz or atazanavir/r were included. Efavirenz participants given increased dose of telaprevir due to drug interaction.
Boceprevir Improves SVR in HCV/HIV Coinfected Subjects

Care of HIV-HCV infected persons

- Vaccinate against HAV and HBV
- In general, treat HIV with ARVs first
- Increased risk of side effects of HIV drugs with HCV treatment
- ARV-HCV treatment drug interactions
- Expected decline in CD4+ T cells on HCV treatment
### Acceptable and Contraindicated Combinations of Hepatitis C Virus (HCV) Protease Inhibitors and Studied HIV Antiretroviral Drugs

<table>
<thead>
<tr>
<th>HCV protease inhibitor and dosage</th>
<th>Acceptable (and alternative) HIV antiretroviral drugs</th>
<th>Contraindicated HIV antiretroviral drugs</th>
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<tbody>
<tr>
<td>Telaprevir 750 mg every 8 hours</td>
<td>• Atazanavir/r</td>
<td>• Lopinavir/r</td>
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<td>• Raltegravir</td>
<td>• Fosamprenavir/r</td>
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<td>• Efavirenz (telaprevir dosage should be increased to 1125 mg every 8 hours)</td>
<td>• Darunavir/r</td>
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<td>Alternatives:</td>
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<td></td>
<td>• Rilpivirine</td>
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Acceptable HIV nucleos(t)ide analogue reverse transcriptase inhibitors include tenofovir, abacavir, emtricitabine, and lamivudine
Side effects of HCV treatment: Anemia

• Anemia is a common side effect of ribavirin, telaprevir and boceprevir. Reducing the ribavirin dose is usual recommended initial management.

• Frequency of anemia with boceprevir (50%) and telaprevir (40%)
Side effects of HCV treatment: peg Interferon alfa

- Fatigue (50%), fever (36%), nausea (23%), muscle aches (37%), joint pains (28%), headache (50%), hair loss (23%), low white count (21%), and low platelets (5%), depression (18%), irritability (13%), less common thyroid disease, rash and increased risk of bacterial infection.
Side effects of Telaprevir

- Rash (56%, severe in 4%) Limiting sun and wearing loose clothes may help
- Anemia (36%)
- Diarrhea
- Anal complaints (hemorrhoids, discomfort, itch)
Side effects of boceprevir

• fatigue
• anemia (48% of boceprevir participants vs 28% in controls)
• nausea, diarrhea, distorted sense of taste
• neutropenia (low white cell count)
How long do HIV-HCV patients need to be treated with telaprevir for HCV?

• No studies to date have evaluated duration of response guided therapy (RGT) in HIV/HCV coinfected persons

• For now treat for 48 weeks (if undetectable HCV RNA at week 4 and 12, can stop telaprevir at week 12 and continue peginterferon alfa and ribavirin for total of 48 weeks)
What is response guided therapy (RGT) and stopping rules for Telaprevir?

• At week 4, patient should have an HCV RNA below 1000 IU/mL. If the HCV RNA is 1000 IU/mL or greater at week 4, all treatment should be stopped.

• If at week 12, the HCV RNA is 1000 IU/mL or greater, all treatment should be stopped.

• At week 24, if the HCV viral load is detectable, peginterferon alfa and ribavirin should be stopped because SVR (cure) is unlikely.
How long do HIV-HCV patients need to be treated with boceprevir for HCV

- All patients with HIV or cirrhosis should be treated with a 4-week lead-in of peginterferon alfa and ribavirin followed by 44 weeks of these 2 drugs and boceprevir (48 weeks total of peginterferon alfa and ribavirin with 44 weeks of boceprevir)

- If the HCV RNA level is above 100 IU/mL at week 12 or is detectable at week 24, treatment should be discontinued
Resistance testing is available but not routinely recommended because of the lack of viable treatment alternatives and clinical outcomes data.

Boceprevir and Telaprevir are highly cross resistant.

New drugs are being studied.
Chronic Hepatitis C Virus Genotype 1

- Fibrosis stage 0 or 1:
  - In general, defer treatment
  - If the patient is a prior relaper, consider treatment with direct-acting antiviral drugs. Studies indicate a high rate of sustained virologic response.

- Fibrosis stage 2:
  - Treat with peginterferon alfa and ribavirin plus a direct-acting antiviral drug.
  - If there is a relative contraindication or there are complicating factors for peginterferon alfa-based therapy, defer therapy.

- Fibrosis stage 3 or 4:
  - Patients with bridging fibrosis or compensated cirrhosis: In general, treat with peginterferon alfa and ribavirin plus a direct-acting antiviral drug. The exception is prior null responders, who have a very low rate of sustained virologic response. The decision of deferral until new therapies are available versus treatment with peginterferon alfa, ribavirin, and telaprevir or boceprevir should be made on a case-by-case basis with HCV treatment experts.

- Patients with decompensated cirrhosis: No treatment is available; refer the patient for liver transplantation evaluation.
Thank you