Hepatitis C Virus and HIV Co-infection 2015 Update

Mia N. Barnes, Pharm.D., BCPS
HIV CPE Training Program for Pharmacists
February 8, 2015
Statement of Disclosure

Presenter has no relevant financial relationships with commercial interests pertaining to the content presented in this program.
Program Objectives

After completing the program, participants should be able to:

1. Explain the impact of HIV on the progression of Hepatitis C co-infection.
2. Improve awareness and understanding of emerging therapies for chronic Hepatitis C genotype 1 infection.
3. Identify potential therapeutic related challenges and clinical considerations associated with treatment of Hepatitis C in the HIV/HCV co-infected patient.
4. Formulate an appropriate management strategy for drug interactions associated with treatment of HIV and HCV.
Hepatitis C

Hepatitis C (HCV) is an RNA virus of the Flaviviridae family.

HCV replicates preferentially in hepatocytes but is not directly cytopathic, leading to persistent infection.

6 genotypes exist, however, there are more than 50 subtypes that may occur.

- Genotype 1 accounts for ~70-75% of U.S. infections.

HCV Replication Cycle
Epidemiology of HCV and HIV Co-Infection

According to the CDC, approximately 3.2 million persons in the United States have chronic HCV infection.

HCV infection occurs commonly among HIV-infected individuals.

Approximately 20% of HIV-infected persons worldwide are estimated to have concurrent chronic HCV infection.

HCV prevalence varies substantially among risk groups, with a prevalence of 50-90% in cohorts of injection drug users in the United States and Europe.

Impact of HIV on the Progression of HCV Co-infection

Morbidity and mortality from infection with HCV in HIV-positive patients are increasing and have become a major challenge in the management of such patients.\(^1\)

A meta-analysis found that HIV/HCV-coinfected patients had a three fold greater risk of progression to cirrhosis or decompensated liver disease than HCV-monoinfected patients.\(^2\)

Rate can be further magnified in HIV/HCV-coinfected patients with low CD4 T lymphocyte cell counts.\(^3\)

3. Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Department of Health and Human Services. Considerations for Antiretroviral Use in Patients with Coinfections
Impact of HIV on the Progression of HCV Co-infection

HCV Acute Infection
- Viral Clearance: 15%-35%
- Chronic Infection: 65%-85%

HIV/HCV co-infected Acute Infection
- Viral Clearance: 5%-10%
- Chronic Infection: 90%-95%

Impact of HCV on the Progression of HIV Co-infection

Co-infection with HIV is a well-recognized contributor to accelerated fibrosis progression.

Chronic infection such as HCV may result to a generalized immune activation

- HIV disease progression may occur through preferential targeting of activated CD4⁴ T cells.

The level of HCV viremia has been shown to inversely correlate with lower CD4 counts and may transiently increase with exposure to ART or alcohol.

Cumulative Survival Free of End-Stage Liver Disease, Hepatocellular Carcinoma, or Death According to Response to Hepatitis C Virus (HCV) Treatment From Baseline in HCV/HIV Co-infected Patients

SVR Is Associated With Improved Survival in HIV/HCV–Coinfected Patients

Log-rank \( P = .005 \)

Screening and Diagnosis of HCV in HIV Positive Patients

KEY CONSIDERATIONS
Screening and Diagnosis of HCV in HIV Positive Patients

HCV Antibody Testing

Positive
- HCV RNA Testing
  - Detectable
    - HCV Infection
  - Undetectable
    - Repeat HCV Antibody test in 4-6 months

Negative
- Check HCV RNA
- Repeat HCV Antibody test in 4-6 months

Adapted from J Acquir Immune Defic Syndr. 2007 Jul 1;45 Suppl 2:S47-56
Treatment of HCV Infection

FOCUSING ON THE HIV/HCV CO-INFECTED POPULATION
Variables to Consider Before Initiating HCV Therapy in HIV-HCV Co-infected Patients

HIV-Related
• CD4 count
• Plasma HIV-RNA
• Antiretrovirals

Liver-Related
• Genotype
• HCV load
• Transaminases
• Histology

Other
• Neuropsychiatric history
• Drug addiction and alcohol consumption

Patient Scenario 1
Co-infected patient who does not require immediate ART and has evidence of liver disease

Ideal scenario, as there is no concern in regard to potential drug interactions. Patient can concentrate on adherence to simpler regimen.

Patient Scenario 2
Co-infected patient with advanced AIDS (CD4<200)

ART and appropriate prophylaxis should be initiated to prevent onset of any opportunistic infections. In patient w/ significant liver disease, HCV therapy should be initiated once CD4 counts have improved and viral suppression is achieved.

Patient Scenario 3
Co-infected patient who meets treatment indications for both infections

Initiate ART first to determine any specific ART related adverse effects. Also, provides clinician and patient opportunity to determine if patient is able to tolerate and adhere to ARV and achieve HIV viral load suppression.

Patient Scenario 4
Co-infected patient with a history of recurrent drug-induced hepatotoxicity

Should be evaluated for underlying liver disease. Consider beginning anti-HCV treatment first and starting ART when biochemical markers improve.

Concurrent Treatment of HIV and Hepatitis C Virus Infection

• Considerations should be made as to pill burden, drug-drug interactions, and toxicities

• Current HIV guidelines state before HCV treatment is initiated the ART regimen may need to be modified to reduce the potential for drug-drug interactions and/or toxicities

• HIV RNA should be measured within 4 - 8 weeks after changing HIV therapy to ensure the effectiveness and safety of the new regimen

• If prior HIV regimen is to be reinitiated after HCV treatment complete, the modified ART regimen should be continued for at least 2 weeks after completion of HCV treatment
Case cont.

TB is a 58 yr old AA male co-infected with HIV/HCV on tenofovir/emtricitabine/efavirenz

- PMH: HIV+ (x10 years), HCV GT 1a, hyperlipidemia, HTN
- Previous IV Drug User x 20 years

<table>
<thead>
<tr>
<th>Laboratory Data</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>ALT: 172</td>
<td>anti-HBs: Positive</td>
<td>CD4: 176</td>
<td></td>
</tr>
<tr>
<td>AST: 179</td>
<td>HBeAg: Negative</td>
<td>HIV PCR RNA: 10,056 copies/mL</td>
<td></td>
</tr>
<tr>
<td>T.bili: 1.2</td>
<td>anti-HBc: Negative</td>
<td>HCV RNA: 3.2 IU/ml</td>
<td></td>
</tr>
<tr>
<td>Alb: 4</td>
<td>anti-HCV: Positive</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Question 1

Would you recommend to initiate HCV treatment in this patient?

a. No, delay treatment since CD4 cells are < 200/μL
b. I believe it would be preferable to continue ART and initiate HCV therapy
c. Discontinue ART therapy and initiate HCV therapy
d. Not sure
Pharmacological Therapies Utilized in the Treatment of HCV Infection
Pegylated-Interferon

2 currently available pegylated interferons

- Peginterferon alfa-2a (Pegasys®)
  - 40-kd branched PEG covalently linked to the standard interferon alfa-2a molecule

- Peginterferon alfa-2b (Peg-Intron)
  - Polyethylene glycol (PEG) covalently linked to the standard interferon alfa-2b molecule
Ribavirin

• Nucleoside analog with broad spectrum antiviral activity
• Inhibits the replication of RNA viruses in cell culture
• Appears to decrease HCV infectivity in a dose-dependent manner
• Should NEVER be used as monotherapy in the treatment of HCV
# Ribavirin Formulations

<table>
<thead>
<tr>
<th>Brand Name</th>
<th>Dosages Available</th>
<th>Special Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ribaspere®</td>
<td>1200 mg, 1000 mg, 800 mg, and 600 mg dose packs</td>
<td>• Provides 7 days of treatment divided into morning and evening doses in efforts to reduce pill burden</td>
</tr>
<tr>
<td>RibaPak®</td>
<td>200 mg, 400 mg, and 600 mg tabs</td>
<td>•</td>
</tr>
<tr>
<td>Rebetol®</td>
<td>200 mg capsule</td>
<td>•</td>
</tr>
<tr>
<td>Rebetol® Oral Solution</td>
<td>40 mg/mL suspension</td>
<td>•</td>
</tr>
<tr>
<td>Copegus®</td>
<td>200 mg tablet</td>
<td>•</td>
</tr>
<tr>
<td>Virazole®</td>
<td>RBV formulation</td>
<td>• Indicated for the treatment of hospitalized infants and young children with severe lower respiratory tract infections due to Respiratory Syncytial Virus (RSV)</td>
</tr>
<tr>
<td>Rebetron®</td>
<td>Combination product of Peg-IFN and RBV</td>
<td>• Discontinued by manufacturer</td>
</tr>
</tbody>
</table>
Warnings Associated with Ribavirin Therapy

• RBV has demonstrated significant teratogenic and/or embryocidal effects in all animal species in which adequate studies have been conducted.

• RBV therapy should not be initiated until confirmation of negative pregnancy test has been obtained immediately prior to planned initiation of therapy.

• Key Clinical Counseling Points
  • Patients should be instructed to use at least two forms of effective contraception during treatment and during the six month period after treatment has been stopped.
  • Pregnancy testing should occur monthly during RBV therapy and for six months after therapy has stopped.
Warnings Associated with Ribavirin Therapy

Hemolytic Anemia is the primary toxicity of RBV

- Approximately one third of patients treated with PEG-IFN/RBV experience anemia, defined as a decrease in hemoglobin level to less than 10 g/dL.[1]
- Reductions in hemoglobin levels occurred within the first 1-2 weeks of oral therapy[2]
- RBV dose reduction is necessary in nearly 30% of patients treated with this regimen[1]

Guidelines for Dose Modifications and Discontinuation for Anemia[2]

<table>
<thead>
<tr>
<th>No Cardiac History</th>
<th>Hgb &lt;10 g/dL</th>
<th>Hgb &lt;8.5 g/dL</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Caveats in the Co-Infected Population: ART & Peg-IFN/Ribavirin Therapy

<table>
<thead>
<tr>
<th>Potential Drug Interactions Between ART &amp; Peg-IFN/RBV Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Didanosine (Videx®)</strong></td>
</tr>
<tr>
<td>-Interaction noted w/ RBV</td>
</tr>
<tr>
<td>-May lead to life-threatening ddI-associated mitochondrial toxicity including hepatomegaly, steatosis, pancreatitis, and lactic acidosis</td>
</tr>
</tbody>
</table>

Targeted Approach to HCV Treatment

HCV Genome Sequence

Hepatitis C virus RNA
9600 nt bases
Gene encoding precursor polyprotein

5’ NTR

Structural proteins
p22
gp35
gp70
p7
p23
p70
p8
p27
p56/58
p68

Envelope glycoproteins
nucleocapsid

C
E1
E2

NS1
NS2
NS3
NS4A
NS4B
NS5A
NS5B

proteases
RNA helicase
transmembrane protein
co-factors
RNA polymerase
interferon resisting protein
HCV DAA Drug Approval Timeline

2011
Incivek®/Victrelis®

Dec. 2013
Olysio®

Oct. 2014
Sovaldi®

Nov. 2014
Harvoni®

Dec. 2014
Olysio®-Sovaldi Combo

Viekira Pak™
NS5B Polymerase Inhibitor

- Direct-Acting Antiretroviral Agents (DAAs):
  - Sofosubvir (SOF/Sovaldi ®)
- Works by inhibition of HCV RNA-dependent RNA polymerase, key enzyme in HCV RNA synthesis
- Nucleotide prodrug that undergoes intracellular metabolism to form the pharmacologically active uridine analog triphosphate (GS-461203)
- Currently FDA indicated for Genotype 1 – 4
  - Including those with hepatocellular carcinoma meeting Milan criteria (awaiting liver transplantation)
  - HCV/HIV-1 co-infection

Clinical Studies of Triple Therapy in the HIV/HCV Co-Infected Population

Sofosbuvir-based therapy: PHOTON-1

Open-label clinical trial evaluating the safety and efficacy of 12 or 24 weeks of treatment

114 HCV Treatment-Naïve Genotype 1 Patients

- Subjects on ART w/ HIV RNA ≤ 50 copies/ml and CD4 ≥ 200
- Subjects not on ART and CD4 ≥ 500

PHOTON-1: SVR 12 with Sofosbuvir + RBV x 12-24 wks

## Caveats in the Co-Infected Population: ART & Sofosbuvir Therapy

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Drug Name</th>
<th>Effect on Concentration of Sofosbuvir or Concomitant Drug</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boosted Protease Inhibitors</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

NS3/4A Serine Protease Inhibitor

• Direct-Acting Antiretroviral Agent (DAA):
  • Simeprevir (SMV/Olysio®)

• Work by inhibition of HCV NS3/4A serine protease
  • HCV NS3/4A protease is necessary for the proteolytic cleavage of the HCV encoded polyprotein into mature forms of the NS4A, NS4B, NS5A and NS5B proteins
  • Essential for viral replication and virion assembly

• Currently only FDA indicated for Genotype 1 HCV
NS3/4A Serine Protease Inhibitor

NS3 Q80K Polymorphism

° Efficacy of simeprevir in combination with peginterferon alfa and ribavirin is greatly decreased in patients who have Genotype 1a Q80K
° Shown to be considerably reduced in two out of three Phase 3 studies in patients with HCV genotype 1a with a baseline Q80K polymorphism
° Baseline testing recommended in all patients

Caveats in the Co-Infected Population: ART & Simeprevir Therapy

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Drug Name</th>
<th>Effect on Concentration of Simeprevir or Concomitant Drug</th>
<th>Recommendations</th>
</tr>
</thead>
</table>
| Non-Nucleoside Reverse Transcriptase Inhibitors | Delavirdine, Etravirine, Nevirapine | ↑ or ↓ simeprevir                                       | • Mechanism due to CYP3A inhibition (delavirdine) or induction (etravirine and nevirapine)  
  • Not recommended to co-administer OLYSIO with delavirdine, etravirine or nevirapine. |
| Pharmacokinetic Enhancer          |                            |                                                         |                                                                                |
| Boosted Protease Inhibitors       | Darunavir/ritonavir        | ↑ simeprevir, ↑ darunavir                                | • Mechanism due to CYP3A inhibition by darunavir/ritonavir                      
  • Coadministration not recommended |
|                                   | All other PIs              | ↑ or ↓ simeprevir                                        | • Mechanism due to CYP3A inhibition or induction by these HIV PIs                
  • Coadministration not recommended with or without ritonavir. |

Harvoni®

Fixed-dose combination FDA indicated for HCV Genotype 1

ledipasvir

sofosbuvir

Clinical Studies of Triple Therapy in the HIV/HCV Co-Infected Population

Ledipasvir-based therapy: NAID ERADICATE trial

Open label study of fixed dose combination of sofosbuvir and ledipasvir

## Caveats in the Co-Infected Population

**ART & Ledipasvir Therapy**

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Drug Name</th>
<th>Effect on Concentration of Ledipasvir or Concomitant Drug</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nucleotide Reverse Transcriptase Inhibitors</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| Boosted Protease Inhibitors                      | tipranavir/ritonavir | ↓ ledipasvir                                              | • Coadministration of HARVONI with tipranavir/ritonavir is expected to decrease the concentration of ledipasvir.  
• Coadministration not recommended              |
Indicated for the treatment of patients with GT1 chronic HCV including those with compensated cirrhosis, HIV/HCV co-infected patients, and patients who have had liver transplant.
Viekira Pak™

Clinical Trials: VIEKIRA PAK™ with or without Ribavirin (RBV) in Chronic Genotype 1

- 97% (n=1053/1084) of patients across multiple GT1 (with or without RBV, 12 weeks vs. 24 weeks depending on patient type) achieved virologic cure*

- Limited Adverse Effects
  - In Phase 3 trials, 1.1 percent (n=20/1804) of patients discontinued treatment when taking VIEKIRA PAK & RBV, while 0.4 percent (n=2/509) d/c treatment when taking VIEKIRA PAK alone

- Reduced Relapse & Virologic Failure
  - Of patients taking the recommended treatment, 1.3 percent (n=14/1068) relapsed and 0.5 percent (n=5/1084) experienced on-treatment virologic failure.

97% Overall Cure (SVR12)

VIEKIRA PAK [package insert]. North Chicago, IL: AbbVie Inc
# VIEKIRA PAK™ Dosing

<table>
<thead>
<tr>
<th>POPULATION</th>
<th>TREATMENT</th>
<th>TREATMENT DURATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genotype 1a, without cirrhosis</td>
<td>VIEKIRA PAK + RBV</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Genotype 1a, w/ cirrhosis</td>
<td>VIEKIRA PAK + RBV</td>
<td>24 weeks</td>
</tr>
<tr>
<td>Genotype 1b, without cirrhosis</td>
<td>VIEKIRA PAK</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Genotype 1b, w/ cirrhosis</td>
<td>VIEKIRA PAK + RBV</td>
<td>12 weeks</td>
</tr>
</tbody>
</table>

VIEKIRA PAK [package insert]. North Chicago, IL: AbbVie Inc
Clinical Studies of Triple Therapy in the HIV/HCV Co-Infected Population

Viekra Pak™-based therapy: TURQUIOSE-1 trial

Open label phase II study to evaluate 12 or 24 wks of treatment w/ Viekira PAK + RBV
Caveats in the Co-Infected Population: VIEKIRA PAK™

In Phase 2 clinical trials, 92 percent of patients co-infected with HCV/HIV-1 achieved SVR12

Risk of HIV-1 Protease Inhibitor Drug Resistance:

RTV component is an HIV-1 protease inhibitor and can select for HIV-1 protease inhibitor resistance

Drug Interactions:

Many considerations must be made when given with HIV Antiviral Agent

Dosing Schedule:

Manufacturer recommends following same dosage recommendations as non-infected patients

VIEKIRA PAK [package insert]. North Chicago, IL: AbbVie Inc
### Caveats in the Co-Infected Population: ART & VIEKIRA PAK™

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Drug Name</th>
<th>Effect on Concentration of Viekira Pak™ or Concomitant Drug</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-Nucleoside Reverse Transcriptase Inhibitors</td>
<td>rilpivirine</td>
<td>↑ rilpivirine</td>
<td>• Coadministration of VIEKIRA PAK with rilpivirine once daily is not recommended, increased risk of QT prolongation</td>
</tr>
<tr>
<td>Boosted Protease Inhibitors</td>
<td>Lopinavir/ritonavir</td>
<td>↑ paritaprevir</td>
<td>• Coadministration not recommended</td>
</tr>
</tbody>
</table>
Comparison of Adverse Effects associated with DAAs

**Sofosbuvir**
- Most common adverse events (≥20%) for SOVALDI + RBV combination therapy were fatigue and headache.
- Most common adverse events (≥20%) for SOVALDI + IFN + RBV combination therapy were fatigue, headache, nausea, insomnia and anemia.

**Simeprevir**
- Most common adverse events (≥20%) receiving the combination of OLYSIO + IFN + RBV: rash (including photosensitivity), pruritus and nausea.

**Harvoni®**
- Incidence greater than or equal to 10%, all grades observed with treatment for 8, 12, or 24 weeks were fatigue and headache.

**Viekira Pak**
- Most common (>10%) w/ RBV: fatigue, nausea, pruritus, other skin reactions, insomnia, and asthenia.
- Adverse reactions (≥5%) w/o RBV were nausea, pruritus, and insomnia.

# FDA-Approved Indications, Dose, Administration, and Drug Cost

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose and Administration&lt;sup&gt;1&lt;/sup&gt;</th>
<th>FDA Approved Indications&lt;sup&gt;1&lt;/sup&gt;</th>
<th>Drug Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sofosbuvir (Sovaldi®)</td>
<td>• 1 tablet daily for 12 weeks</td>
<td>HCV genotype 1, 2, 3 or 4 infection, including those with hepatocellular carcinoma meeting Milan criteria (awaiting liver transplantation) and those with HCV/HIV-1 co-infection</td>
<td>$84,000 for 12 weeks sofosbuvir</td>
</tr>
<tr>
<td>Simeprevir (Olysio®)</td>
<td>• 1 tablet daily for 12 weeks</td>
<td>HCV genotype 1 in combination with peginterferon alfa and ribavirin in subjects with compensated liver disease (including cirrhosis) Must be used in combination w/ peg-IFN and ribavirin</td>
<td>$66,360 for 12 weeks simeprevir</td>
</tr>
<tr>
<td>Ledipasvir/Sofosbuvir (Harvoni®)</td>
<td>• 90 mg ledipasvir and 400 mg sofosbuvir daily 12-24 weeks</td>
<td>HCV genotype 1 infection in adults</td>
<td>$94,500</td>
</tr>
<tr>
<td>Ombitasvir, paritaprevir, ritonavir; and dasabuvir (Viekira Pak™)</td>
<td>• 2 ombitasvir/paritaprevir/RTV 12.5/75/50 mg tablets once daily (in the morning) and 1 dasabuvir 250 mg tablet twice daily (morning and evening)</td>
<td>With or without ribavirin (RBV), is indicated for the treatment of adult patients with genotype 1 chronic hepatitis C virus infection, including those with compensated cirrhosis.</td>
<td>$83,320 (12 wks) $167,640 (24 wks)</td>
</tr>
</tbody>
</table>

Product labels with prescribing information for sofosbuvir, simeprevir, Harvoni®, Viekira Pak™.
HIV/HCV-coinfected persons should be treated and retreated the same as persons without HIV infection, after recognizing and managing interactions with antiretroviral medications.
### Summary of Recommendations for HIV/HCV-Coinfected Patients Who are Being Treated for HCV GT-1a

<table>
<thead>
<tr>
<th>Recommended</th>
<th>Alternative</th>
<th>NOT Recommended</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Treatment naive</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ledipasvir/sofosbuvir x 12 weeks</td>
<td>Sofosbuvir + weight-based RBV x 24 wks</td>
<td></td>
</tr>
<tr>
<td>Rating: Class I, Level A</td>
<td>Rating: Class I, Level A</td>
<td></td>
</tr>
<tr>
<td>Paritaprevir/ombitasvir/RTV + dasabuvir + weight-based RBV x 12 wks (no cirrhosis) or 24 weeks (cirrhosis)</td>
<td>PEG-IFN+ RBV w/ or w/o sofosbuvir, simeprevir, telaprevir, or boceprevir for 12 wks to 48 wks</td>
<td></td>
</tr>
<tr>
<td>Rating: Class I, Level A</td>
<td>Rating: Class IIb, Level A</td>
<td></td>
</tr>
<tr>
<td>Sofosbuvir + simeprevir with or without weight-based RBV x12 wks (no cirrhosis) or 24 weeks (cirrhosis)</td>
<td>Monotherapy with PEG-IFN, RBV, or a direct-acting antiviral</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Rating: Class III, Level A</td>
<td></td>
</tr>
</tbody>
</table>

## Summary of Recommendations for HIV/HCV-Coinfected Patients Who are Being Treated for HCV GT-1a+1b

<table>
<thead>
<tr>
<th>Recommended</th>
<th>Alternative</th>
<th>NOT Recommended</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Treatment experienced (No cirrhosis)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ledipasvir/sofosbuvir x 12 weeks Rating: Class I, Level A</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paritaprevir/ombitasvir/RTV + dasabuvir + weight-based RBV x 12 wks Rating: Class I, Level A</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sofosbuvir + simeprevir with or without weight-based RBV x12 wks</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sofosbuvir + weight-based RBV x 24 wks Rating: Class IIb, Level A</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PEG-IFN+ RBV w/ or w/o sofosbuvir, simeprevir, telaprevir, or boceprevir for 12 wks to 48 wks Rating: Class IIb, Level A</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monotherapy with PEG-IFN, RBV, or a direct-acting antiviral Rating: Class III, Level A</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Caveats in the Co-Infected Population: Recommendations related to HCV drug interactions with HIV ARVs

• Fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg):
  • Ledipasvir increases tenofovir levels
  • Concomitant use mandates consideration of creatinine clearance (CrCl) rate and should be avoided in those with CrCl below 60 mL/min.,
  • Ledipasvir should be avoided with this combination (pending further data) unless antiretroviral regimen cannot be changed and the urgency of treatment is high

• Rating: Class IIa, Level C

• For combinations expected to increase tenofovir levels, baseline and ongoing assessment for tenofovir nephrotoxicity is recommended.

• Rating: Class IIa, Level C

Caveats in the Co-Infected Population: Recommendations related to HCV drug interactions with HIV ARVs

• Daily fixed-dose combination of Viekira Pak™:
  • Paritaprevir/ritonavir/ombitasvir plus dasabuvir should be used with antiretroviral drugs with which it does not have substantial interactions: raltegravir (and probably dolutegravir), enfuvirtide, tenofovir, emtricitabine, lamivudine, and atazanavir

• The dose of ritonavir used for boosting of HIV protease inhibitors may need to be adjusted (or held) when administered with paritaprevir/ritonavir/ombitasvir plus dasabuvir and then restored when HCV treatment is completed

• HIV protease inhibitor should be administered at the same time as the fixed-dose HCV combination

• Rating: Class IIa, Level C

Caveats in the Co-Infected Population:
Recommendations related to HCV drug interactions with HIV ARVs

• Simeprevir:
  • Simeprevir should only be used with antiretroviral drugs with which it does not have clinically significant interactions
  • Raltegravir (and probably dolutegravir), rilpivirine, maraviroc, enfuvirtide, tenofovir, emtricitabine, lamivudine, and abacavir.
  • Rating: Class IIa, Level B

Caveats in the Co-Infected Population:
Recommendations related to HCV drug interactions with HIV ARVs

Antiretroviral treatment interruption to allow HCV therapy is NOT recommended.

Rating: Class III, Level A

Case cont.

Six months later the patient’s CD4 count and HIV viral load have improved. Liver biopsy revealed presence of portal fibrosis. Treatment was initiated with Viekira Pak™. However, transaminases have continued to elevate.

Medications:

• Tenofovir/emtricitabine 300/200 mg PO qDaily
• Efavirenz (Sustiva®) 600 mg PO qHS
• Viekira Pak™ as directed

<table>
<thead>
<tr>
<th>Laboratory Data</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>ALT: 185 IU/L</td>
<td>WBC: 6500/mm³</td>
</tr>
<tr>
<td>AST: 175 IU/L</td>
<td>Hbg = 14 g/dL</td>
</tr>
<tr>
<td>Tbili.:0.6 mg/dL</td>
<td>Plt:165,000/μL</td>
</tr>
<tr>
<td>Albumin = 2.2 g/dL</td>
<td>HCV RNA Log 2.2 IU/mL</td>
</tr>
<tr>
<td></td>
<td>HCV genotype 1A</td>
</tr>
</tbody>
</table>
Question 5

As the pharmacist reviewing this patient’s current medications what should be our concern at this point?

A. Lamivudine/zidovudine 150/300 mg PO BID
B. Efavirenz 600 mg PO qHS
C. Viekira Pak™
D. B & C
E. All of the Above
Challenges Associated With HCV Treatment in the HIV Infected Population: Where Are We Now?

Positive Considerations

Negative Considerations

DRUG INTERACTIONS

- Drug-drug interactions
- Potential for re-infection

POTENTIAL FOR RE-INFECTION

- High SVR rates observed in co-infected patients
- Treatment may limit progressive to further liver injury or death

COST

- Treatment may be costly
- Still risk of poor response
- No FDA indication for HIV+ patients
PROGRAM & PRESENTER EVALUATION

PLEASE COMPLETE THE PROVIDED PROGRAM AND PRESENTER EVALUATION SURVEY THAT CAN BE FOUND ONLINE. SUBMISSION OF THESE DOCUMENTS IS REQUIRED FOR RECEIVING CONTINUING PHARMACY EDUCATION CREDIT.

THANK YOU