Financial Disclosure

None

(Updated March 8, 2016)
Learning Objectives

1. Discuss the epidemiology of hepatitis C and populations at risk for hepatitis C infection
2. Identify consequences of untreated Hepatitis C, including cirrhosis and HCC
3. Recognize the different treatment options for hepatitis C infection in HIV infected individuals
CDC Testing Recommendations


- Adults born from 1945 through 1965
- Currently injecting or ever injected drugs
- Received clotting factors made before 1987
- Received blood/organs before July 1992
- Were ever on chronic hemodialysis
- Have persistent abnormal alanine aminotransferase levels (ALT)
- HIV infection
CDC Testing Recommendations


- HCV-testing based on recognized exposure:
  - Healthcare, emergency, and public safety workers after exposure (needle stick/mucosal)
  - Children born to HCV-positive mothers
  - Persons who might have been exposed to HCV within the past six months
HCV Testing Algorithm


EIA for anti-HCV

HCV RNA

+  

HCV RNA

+  

RIBA*

Resolved HCV Infection

Active HCV Infection
Medical Evaluation

-  

Negative for HCV Infection
Additional Testing Recommended if:
• Acute HCV suspected
• Hemodialysis
• Immunocompromised

-  

False-Reactive EIA

*Alternatively, the EIA signal-to-cut-off ratio could be used in place of the RIBA in patients with positive EIA and negative HCV RNA:
- High signal/cut-off ratio indicates resolved HCV infection
- Low signal/cut-off ratio indicates false-reactive EIA
Hepatitis C Testing

WHO Executive Summary on HCV 2014

- HCV RNA can be detected as early as 2-3 weeks after infection
- EIA anti-HCV screening test may detect HCV infection 4-10 weeks after infection
- Anti-HCV can be detected in > 97% of persons by 6 months after exposure
- Prior infection with HCV does not protect against later infection with the same or different genotypes of the virus
- Superinfection with more than one genotype of HCV is possible
Natural History of HCV Infection

- **Exposure (Acute Phase)**
  - 15% (15)Resolved
  - 85% (85)Chronic
    - 80% (68)Stable
    - 20% (17)Cirrhosis
      - 75% (13)Slowly Progressive
      - 25% (4)HCC Transplant Death

From: emedicine.medscape.com/article/177792; accessed 02/26/2016
Complications related to Chronic HCV  

- Diabetes mellitus
- Glomerulonephritis
- Essential mixed cryoglobulinemia
- Porphyria cutanea tarda
- Lichen planus
- Non-Hodgkins lymphoma
- Thyroid disorders
Management of Hepatitis C

- Screen for alcohol use
- Provide counseling to reduce moderate and high levels of alcohol intake
- Assess use of other drugs
- Address co-morbidities (smoking and high body mass index)
- Assess risk for transmission
Management of Hepatitis C

• Evaluate for the presence of chronic liver disease
  ◦ Liver function tests
  ◦ Severity of liver disease
  ◦ Need for treatment
  ◦ Viral genotyping

• Assess the need for Hepatitis A and Hepatitis B vaccine
HCV–Infected Persons in the US and Estimated Rates of Detection, Referral to Care, and Treatment

5-Year Risk of All-cause Mortality: SVR24 versus Non-SVR24

• Significant survival benefit with achieving SVR24
• Adjusted hazard ratios for mortality: SVR vs Non-SVR (95% CI)
  • General: 0.33 (0.23 - 0.46)
  • Cirrhotic: 0.26 (0.18 - 0.37)
  • HCV/HIV: 0.21 (0.10 – 0.45)
• Research needed
  • Prospective data with newer medications

VA HCV Clinical Case Registry (1999-2009): Incidence and Predictors of HCC after SVR
El-Serag HB, *Hepatology*. 2016;March 4 (Epub ahead of print)

• Retrospective cohort study (n=10,817)

• Incidence of HCC (per 1000 patient-years)
  - With SVR: 3.27 (0.327%/year)
  - No SVR: 13.2 (1.32%/year)

• SVR Cohort (no HCC, pegIFN + RBV)
  - Mean age (53 years; 12% > 60 years of age), male (95%), black (13%), non-Hispanic white (64%), Hispanic (3%)
  - New HCC cases post SVR (n=100 during 30,562 person-years, median 2.8 years after SVR)
HCV genome and Potential Drug Targets
Asselah T, Proced Hep Conf, Vol 33, s1, Feb 2013
Assessment of Liver fibrosis

- Clinical scores (MELD, Child-Pugh's)
- Serum markers and panels: Fibrotest®, Hepascore®, FibroSpect®, ELF score®, AAR, APRI, FIB-4, etc.
- Transient Elastography (Fibroscan®)
- Hepatic venous pressure gradient (HVPG)
- Liver imaging: Ultrasound, CT scan, MRI of the liver
FibroScan® Score

F0/F1
NO, OR MILD FIBROSIS
Indicates no or minimal liver fibrosis and no evidence of progressive liver disease

F2
MODERATE FIBROSIS
Indicates significant liver fibrosis and evidence of progressive liver disease

F3
SEVERE FIBROSIS
Indicates severe liver fibrosis and high risk progression to cirrhosis

F4
CIRRHOSIS
Indicates extensive liver fibrosis consistent with cirrhosis
FibroScan® Scoring Card

CORRELATION BETWEEN LIVER STIFFNESS (kPa) & FIBROSIS STAGE

- Hepatitis B*
- HCV-HIV co-infection*
- Hepatitis C recurrence after liver transplantation*
- Hepatitis C*
- Chronic cholestatic diseases*
- Alcohol**
- NAFLD***

LIVER DISEASE

LIVER STIFFNESS (kPa)

0 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 75

- F0
- F0-F1
- F1
- F1-F2
- F2
- F2-F3
- F3
- F3-F4
- F4
<table>
<thead>
<tr>
<th>Fibrosis Score</th>
<th>Activity Score</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>F0</strong> No fibrosis</td>
<td><strong>A0</strong> No activity</td>
</tr>
<tr>
<td><strong>F1</strong> Portal fibrosis without septa</td>
<td><strong>A1</strong> Mild activity</td>
</tr>
<tr>
<td><strong>F2</strong> Portal fibrosis with few septa</td>
<td><strong>A2</strong> Moderate activity</td>
</tr>
<tr>
<td><strong>F3</strong> Numerous septa without cirrhosis</td>
<td><strong>A3</strong> Severe activity</td>
</tr>
<tr>
<td><strong>F4</strong> Cirrhosis</td>
<td></td>
</tr>
</tbody>
</table>
## Initial Treatment of HCV: Genotype 1a

<table>
<thead>
<tr>
<th>Treatment Naïve</th>
<th>Without Cirrhosis (Weeks)</th>
<th>Compensated Cirrhosis (Weeks)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GZR/EBV*</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>LED/SOF</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>PrOD + RBV</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>SMP + SOF</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>DCV + SOF</td>
<td>12</td>
<td></td>
</tr>
</tbody>
</table>

*if no baseline high fold-change NS5A RAV for elbasvir are detected

## Initial Treatment of HCV: Genotype 1a (Alternative)

<table>
<thead>
<tr>
<th>Treatment Naïve</th>
<th>Without Cirrhosis (Weeks)</th>
<th>Compensated Cirrhosis (Weeks)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GZR/EBV* + RBV</td>
<td>16</td>
<td>16</td>
</tr>
<tr>
<td>LED/SOF</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>PrOD + RBV</td>
<td></td>
<td>24</td>
</tr>
<tr>
<td>SMP + SOF + RBV</td>
<td></td>
<td>24</td>
</tr>
<tr>
<td>DCV + SOF + RBV</td>
<td></td>
<td>24</td>
</tr>
</tbody>
</table>

*if baseline high fold-change NS5A RAV for elbasvir are detected

# HCV NS5A Drug Resistance Assay

**Monogram Biosciences**

LabCorp Specialty Testing Group

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**Patient Information**

- **Patient Name**:
- **DOB**:
- **Patient ID/Medical Record #**:
- **Gender**:
- **Monogram Assession #**:
- **Date Collected**:
- **Date Received**:
- **Date Reported**:  
- **Mode**:  
- **Report Status**:  
- **Referring Physician**:  
- **Comments**:  

---

**Drug**

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Brand Name</th>
<th>Region</th>
<th>Drug Resistance Associated Mutations Detected</th>
<th>Drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ledipasvir</td>
<td>ledipasvir</td>
<td>NS5A</td>
<td>L31M, Y93H</td>
<td>LDV</td>
</tr>
<tr>
<td>Ombitasvir</td>
<td>ombitasvir</td>
<td>NS5A</td>
<td>L31M, Y93H</td>
<td>OBV</td>
</tr>
</tbody>
</table>

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**Assessment**

- **Resistant**

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**Important Definitions**

- All mutations are reported relative to the HCV genotype/subtype specific reference Con 1
- Assessment of drug susceptibility is based on detected mutations and is interpreted using a rules-based algorithm (version 3)
- Hepatitis C virus resistance-associated polymorphisms identified at baseline may impact sustained virologic response rates if the treatment regimen, or adherence, is suboptimal. The impact of these polymorphisms may vary in treatment-naïve compared to treatment-experienced populations and according to disease status.

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**Summary of All Mutations Observed**

<table>
<thead>
<tr>
<th>Region</th>
<th>Genotype</th>
<th>Summary of All Mutations Observed</th>
</tr>
</thead>
</table>

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*For more information on interpreting this report, please call Monogram Customer Service at 800-777-0177 between the hours of 6:30am to 5:00pm Pacific Time Monday through Friday.*

*This assay is a next-generation sequence-based resistance assay that analyzes the specified non-structural coding regions of HCV genotypes 1a or 1b. Genotype assignment is determined from the sequence of the specified regions that are derived using subtype-specific methodology, and should not be used to establish or confirm the HCV genotype. HCV genotype determination should only be done with an assay intended for that purpose. This assay meets the standards for performance characteristics and all other quality control and assurance requirements established by the Clinical Laboratory Improvement Amendments. This assay was validated by testing samples with viral loads equal to or above 800 IU/mL, and should be interpreted only on such specimens. The results should not be used as the sole criteria for patient management. The results have been disclosed to you from confidential records protected by law and are not to be disclosed to unauthorized persons. Further disclosure of these results is prohibited without specific consent of the person, to whom it pertains, or as permitted by law.*

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**Page 1 of 1**

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*Southeast AIDS Education & Training Center*

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*University of Miami Miller School of Medicine*
# Initial Treatment of HCV: Genotype 1b

<table>
<thead>
<tr>
<th>Treatment Naïve</th>
<th>Without Cirrhosis (Weeks)</th>
<th>Compensated Cirrhosis (Weeks)</th>
</tr>
</thead>
<tbody>
<tr>
<td>EBV/GZR</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>LED/SOF</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>PrOD + RBV</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>SMP + SOF</td>
<td>12</td>
<td>(± RBV) 24</td>
</tr>
<tr>
<td>DCV + SOF</td>
<td>12</td>
<td>(± RBV) 24</td>
</tr>
</tbody>
</table>

## Outcomes with AASLD-IDSA Recommended HCV Regimens for Genotype 1 Patients

<table>
<thead>
<tr>
<th>Treatment Status</th>
<th>SVR 12 Rate (%)</th>
<th>Relapse Rate (%)</th>
<th>Discontinuation due to Adverse Events (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Treatment naïve:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No-cirrhosis</td>
<td>97 – 99</td>
<td>0 – 3</td>
<td>0 – 1</td>
</tr>
<tr>
<td>Compensated cirrhosis</td>
<td>88 – 100</td>
<td>&lt;1 – 6</td>
<td>0 – 3</td>
</tr>
<tr>
<td><strong>PegIFN/RBV-experienced:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No-cirrhosis</td>
<td>95 – 100</td>
<td>0 – 5</td>
<td>0 – 3</td>
</tr>
<tr>
<td>Compensated cirrhosis</td>
<td>79 – 99</td>
<td>1 – 19</td>
<td>0 – 3</td>
</tr>
<tr>
<td>Decompensated cirrhosis</td>
<td>81 – 92</td>
<td>8</td>
<td>3 – 17</td>
</tr>
</tbody>
</table>

# Initial Treatment of HCV: Genotype 2

<table>
<thead>
<tr>
<th>Treatment Naïve</th>
<th>Without Cirrhosis (Weeks)</th>
<th>Compensated Cirrhosis (Weeks)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SOF + RBV</td>
<td>12</td>
<td>16 - 24</td>
</tr>
<tr>
<td>DCV + SOF</td>
<td>12</td>
<td>16</td>
</tr>
</tbody>
</table>

# Initial Treatment of HCV: Genotype 3

<table>
<thead>
<tr>
<th>Treatment Naïve</th>
<th>Without Cirrhosis (Weeks)</th>
<th>Compensated Cirrhosis (Weeks)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DCV + SOF</td>
<td>12</td>
<td>(± RBV) 24</td>
</tr>
<tr>
<td>SOF + RBV + PEG-IFN</td>
<td>12</td>
<td>12 - 24</td>
</tr>
</tbody>
</table>

## Initial Treatment of HCV: Genotype 4

<table>
<thead>
<tr>
<th>Treatment Naïve</th>
<th>Without Cirrhosis (Weeks)</th>
<th>Compensated Cirrhosis (Weeks)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GZR/EBV*</td>
<td>12</td>
<td>12</td>
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<tr>
<td>LED/SOF</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>PrOD + RBV</td>
<td>12</td>
<td>12</td>
</tr>
</tbody>
</table>

# Initial Treatment of HCV: Genotype 5/6

<table>
<thead>
<tr>
<th>Treatment Naïve</th>
<th>Without Cirrhosis (Weeks)</th>
<th>Compensated Cirrhosis (Weeks)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LED/SOF</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>SOF + RBV + PEG-IFN</td>
<td>12</td>
<td>12</td>
</tr>
</tbody>
</table>

Drug-drug interactions between HCV DAAs and HIV ARV

<table>
<thead>
<tr>
<th>NRTIs</th>
<th>SIM</th>
<th>DCV</th>
<th>SOF</th>
<th>SOF/LDV</th>
<th>3D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abacavir</td>
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<tr>
<td>Emtricitabine</td>
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<tr>
<td>Lamivudine</td>
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<tr>
<td>Tenofovir</td>
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<tr>
<td>Zidovudine</td>
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</table>

<table>
<thead>
<tr>
<th>NNRTIs</th>
<th>SIM</th>
<th>DCV</th>
<th>SOF</th>
<th>SOF/LDV</th>
<th>3D</th>
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</thead>
<tbody>
<tr>
<td>Efavirenz</td>
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<tr>
<td>Etravirine</td>
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<tr>
<td>Nevirapine</td>
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<tr>
<td>Rilpivirine</td>
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</tbody>
</table>
# Drug-drug interactions between HCV DAAs and HIV ARV

<table>
<thead>
<tr>
<th>Protease Inhibitors</th>
<th>SIM</th>
<th>DCV</th>
<th>SOF</th>
<th>SOF/LDV</th>
<th>3D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atazanavir; ATVr; Atazanavir/cobicistat</td>
<td></td>
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<td></td>
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<tr>
<td>Darunavir/ritonavir; darunavir/cobicistat</td>
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<tr>
<td>Lopinavir</td>
<td></td>
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<tr>
<td>Entry/Integrase inhibitors</td>
<td></td>
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<tr>
<td>Dolutegravir</td>
<td></td>
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<tr>
<td>Elvitegravir/cobi</td>
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<tr>
<td>Maraviroc</td>
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<tr>
<td>Raltegravir</td>
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</table>
Summary

• New direct-acting oral antivirals agents are capable of curing HCV infection

• HIV/HCV-coinfected patients have from more liver-related morbidity and mortality, nonhepatic organ dysfunction, and overall mortality than HCV-monoinfected patients

• People with HCV who have cirrhosis at the time they achieve an SVR require long-term monitoring for liver cancer
Questions?
This Presentation and resources are made possible by AETC grant award U1OHA29295 from the HIV/AIDS Bureau of the Health Resources Services Administration (HRSA), U. S. Department of Health and Human Services (HHS).

The information presented is the consensus of HIV/AIDS specialists within the SEAETC and does not necessarily represent the official views of HRSA/HAB.

The AIDS Education and Training Center (AETC) Program is the training arm of the Ryan White HIV/AIDS Program. The AETC Program is a national network of leading HIV experts who provide locally based, tailored education, clinical consultation and technical assistance to healthcare professionals and healthcare organizations to integrate high quality, comprehensive care for those living with or affected by HIV.
Florida Counties
The U.S. Department of Health and Human Services (DHHS) has released updated versions of its antiretroviral treatment guidelines for adults and adolescents, and for children with HIV. The new adult guidelines include revised recommendations for first-line antiretroviral therapy (ART) as well as management of treatment-experienced patients. The revised pediatric guidelines include a discussion of very early treatment for HIV-infected infants.

References
HHS Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents. Updated April 8, 2015.
TRAINING OPPORTUNITIES

Preceptorships
An intensive clinical training program offered to healthcare providers in Florida who have an interest in learning more about the diagnosis and management of HIV/AIDS, opportunistic infections, and co-morbid conditions. Each preceptorship is structured to meet the unique needs of the individual participant based on his or her previous experience, geographic location, and time available. Experience 4 to 240 hours of clinical training at adult, pediatric, obstetric, and/or family practice clinics where care is provided to HIV-infected patients. All training provided is consistent with current guidelines from the Department of Health and Human Services or other nationally recognized guidelines when available.

Clinical Consultation
Individual and group clinical consultations are offered. Individual clinical case consultation is provided on the diagnosis, prevention, and treatment of HIV/AIDS and related conditions. These consultations take place by telephone, email or face-to-face meetings. Group clinical consultation with case-based discussions include information on pharmacology, clinical antiretroviral therapy updates, drug-drug interactions, and antiretroviral resistance.
FOR MORE INFORMATION, PLEASE VISIT:
http://hivaidsinstitute.med.miami.edu/partners/se-aetc
National HIV/AIDS Clinicians’ Consultation Center
UCSF – San Francisco General Hospital

**Warmline**
National HIV/AIDS Telephone Consultation Service
*Consultation on all aspects of HIV testing and clinical care*
Monday - Friday
9 am – 8 pm EST
Voicemail 24 hours a day, 7 days a week

**PEPline**
National Clinicians’ Post-Exposure Prophylaxis Hotline
*Recommendations on managing occupational exposures to HIV and hepatitis B & C*
9 am - 2 am EST, 7 days a week

**Perinatal HIV Hotline**
National Perinatal HIV Consultation & Referral Service
*Advice on testing and care of HIV-infected pregnant women and their infants*
*Referral to HIV specialists and regional resources*
24 hours a day, 7 days a week

HRSA AIDS ETC Program & Community Based Programs, HIV/AIDS Bureau & Centers for Disease Control and Prevention (CDC)
www.nccc.ucsf.edu
NEXT WEBINARS

APRIL 7th
Assessing the HIV Patient
DR. JEFFREY BEAL

APRIL 14th
Management of the ARV Naïve Patient
DR. MESFIN FRANSUA

APRIL 22nd
STD Update
DR. JOSE CASTRO
Need Additional Information?

Contact the South FL SE AIDS Education and Training Center

Franklin Monjarrez, Program Manager: fbm20@med.miami.edu

Tivisay Gonzalez, Program Coordinator: tgonzalez1@med.miami.edu
Target audience: Physicians, physician assistants, nurses, pharmacists, social workers, mental health workers, nutritionist/dietitians.

The Suwannee River Area Health Education Center, Inc. is a Florida Board of Nursing, Dentistry, Pharmacy, Psychology, Respiratory Care, Occupational Therapy, Nursing Home Administration, Clinical Social Work, Marriage and Family Therapy and Mental Health Counseling and Florida Council of Dietetics and Nutrition approved provider of continuing education. CE Broker Provider ID #50-1922.

This program meets the requirements for up to 1.0 contact hours. The Florida AHEC Network designates this live activity for a maximum of 1.0 AMA PRA Category 1 Credits™.
We thank you for participating in today’s webinar and encourage you to stay on WebEx and fill out the Performance Evaluation after the call ends. This is a HRSA requirement that helps us ensure continued funding.
Thank you!