ACTHIV
THE AMERICAN CONFERENCE FOR THE TREATMENT OF HIV

ACTHIV 2017: A State-of-the-Science Conference for Frontline Health Professionals
Meet the Professor: HIV/HCV Coinfection

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University of Pennsylvania
Learning Objectives

Upon completion of this presentation, learners should be better able to:

• Identify the necessary HCV pre-treatment evaluations for HIV/HCV-coinfected patients

• Explain the importance of staging liver fibrosis in HIV/HCV

• Review current HCV treatment options for HIV/HCV patients

• Consider antiretroviral-HCV drug-drug interactions when adding HCV therapy to the regimen of a coinfected patient

• Appraise HCV treatment options for HIV/HCV patients with renal impairment
Case 1: 54 yo Woman with HIV and Genotype 1a Chronic HCV

- HIV (4/2008):
  - Risk factor: IV drug use
  - Elvitegravir/cobicistat/tenofovir (TDF)/emtricitabine
  - 1/2016: CD4 741/mm³ (28%); HIV 0 copies/mL

- HCV antibody-positive (4/2008):
  - HCV genotype 1a; HCV RNA 6.8 log IU/mL
  - Liver biopsy (11/2008): stage 1 fibrosis, steatosis
  - Never treated for chronic HCV
Case 1: 54 yo Woman with HIV and Genotype 1a Chronic HCV

- Past History: hyperlipidemia, acid reflux
- Medications:
  - Elvitegravir/cobicistat/tenofovir (TDF)/emtricitabine
  - Atorvastatin, omeprazole
- Social History:
  - Past IV heroin, cocaine use (1996-2008)
  - Drinks 1 glass of wine 4 times/week
Case 1: 54 yo Woman with HIV and Genotype 1a Chronic HCV

- Physical exam:
  - Ht 5’9”; Wt 94 kg; BMI 28.8 kg/m²
  - No hepatomegaly, stigmata of liver disease

- Laboratory data:
  - TB 0.8; Alb 3.8; INR 1.1; ALT 98; AST 76
  - WBC 6.3; Hgb 13.9; platelets 98; Cr=0.98
  - HAV IgG (+)
  - HBV sAg (-); anti-HBc (+); anti-HBs (+)
Question: What Would You Do Next?

A. Monitor her, she had stage 1 fibrosis
B. Initiate elbasvir/grazoprevir
C. Stage her liver fibrosis
D. Initiate sofosbuvir/ledipasvir
Insert Web Page

This app allows you to insert secure web pages starting with https:// into the slide deck. Non-secure web pages are not supported for security reasons.

Please enter the URL below.

https://api.cvent.com/polling/v1/api/polls/spr30rxd

Note: Many popular websites allow secure access. Please click on the preview button to ensure the web page is accessible.
HCV Pre-Treatment Evaluation in HIV

- Prior HCV treatment, outcome
- Pregnancy screen
- Alcohol, drug use
- ART, non-ARV drugs (drug-drug interactions)
- Laboratory:
  - HCV RNA, genotype (GT)/subtype, NS5A RAS
  - ALT, AST, total bilirubin, albumin, INR
  - Blood count (platelets), creatinine, HIV RNA, CD4
  - Hepatitis A, hepatitis B serologies
  - Stage of liver fibrosis (advanced fibrosis/cirrhosis?)

www.hcvguidelines.org
HCV Pre-Treatment Evaluation in HIV

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  - Hepatitis A, hepatitis B serologies
  - Stage of liver fibrosis (advanced fibrosis/cirrhosis?)
Staging HCV Liver Fibrosis

• Important part of chronic HCV work-up

• Identify advanced hepatic fibrosis/cirrhosis:
  – Strongly consider antiviral therapy
  – Influences treatment duration
  – ↑ hepatocellular ca risk: need to screen
  – Monitor for varices (endoscopy), decompensation
How to Determine Liver Fibrosis Stage

**Liver Biopsy**

**Serum Markers**

FIB-4 = \( \frac{\text{age (years)} \times \text{AST (U/L)}}{\text{platelets (10}^9/\text{L}) \times \sqrt{\text{ALT (U/L)}}} \)

APRI = \( \frac{\text{AST (U/L)}}{\text{AST (upper limit normal)}} \times \frac{1}{\text{platelets (10}^9/\text{L})} \times 100 \)

**Transient Elastography**

Ultrasound

Liver stiffness (kPa)

Liver fibrosis

Risk of ESLD in HIV/HCV Patients on ART, By FIB-4 and Race

A. Non-blacks

<table>
<thead>
<tr>
<th>FIB-4 Score</th>
<th>Risk of ESLD Over Time</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 Yr</td>
</tr>
<tr>
<td>&lt;1.45</td>
<td>0.2%</td>
</tr>
<tr>
<td>1.45-3.25</td>
<td>0.4%</td>
</tr>
<tr>
<td>&gt;3.25</td>
<td>8%</td>
</tr>
</tbody>
</table>

B. Blacks

<table>
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<tr>
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<td>1.45-3.25</td>
<td>0.5%</td>
</tr>
<tr>
<td>&gt;3.25</td>
<td>2%</td>
</tr>
</tbody>
</table>

Care of HCV Patients With Cirrhosis

- Hepatocellular carcinoma (HCC) screening
  - Liver ultrasound every 6 months

- Endoscopy: identify esophageal varices
  - Initiate beta-blocker if present

- Determine if compensated or decompensated
  - Child-Pugh: encephalopathy, ascites, bilirubin, albumin, INR
  - Hepatology referral

- Monitor for complication of cirrhosis

Complications of Cirrhosis

Hepatic Decompensation Events

- Ascites/Peritonitis
- Variceal Hemorrhage
- Hepatic Encephalopathy

Primary Liver Cancer

- Hepatocellular Carcinoma (HCC)
Additional Chronic HCV Counseling

- Hepatitis A, B immunizations if non-immune
- Anti-HBV ART if HBV-coinfected
- Abstain from alcohol
- Maintain BMI <25 kg/m²
- Limit acetaminophen to <2 gm/day
- Avoid raw seafood (*Vibrio* infection)
Case 1: 54 yo Woman with HIV and Genotype 1a Chronic HCV

- Transient elastography → stage liver fibrosis
Case 1: 54 yo Woman with HIV and Genotype 1a Chronic HCV

- Liver stiffness measure = 14.2 kPa (F4) → cirrhosis

http://hepcbc.ca/tests/non-invasive-tests/fibroscan/
Case 1: 54 yo Woman with HIV and Genotype 1a Chronic HCV

- FIB-4 = 3.55 (26% risk of ESLD in 5 years)
- Made decision to abstain from alcohol
- Abdominal ultrasound: no masses, ascites
- Endoscopy: varices $\rightarrow$ nadolol
- Wants to initiate HCV therapy
Question: What Do You Need to Do in Anticipation of HCV Therapy?

A. Nothing, prescribe elbasvir/grazoprevir
B. Clarify dose of atorvastatin
C. Modify ART in advance of HCV treatment
D. Clarify dose, administration of omeprazole
What Would You Do Next?

- Monitor her, she had stage 1 fibrosis: 0%
- Initiate elbasvir/grazoprevir: 0%
- Stage her liver fibrosis: 0%
- Initiate sofosbuvir/ledipasvir: 0%

Source: https://api.event.com/polling/41/api/polls/annd30rd
Factors to Consider in Selection of a DAA Regimen

- HCV genotype
- Cirrhosis
- Drug-drug interactions
- Renal impairment
- Prior treatment experience (esp. DAAs)
- Insurance → Which DAA is on formulary?
# Antiretroviral-DAA Drug-Drug Interactions

<table>
<thead>
<tr>
<th>ARV</th>
<th>Elbasvir/Grazoprevir</th>
<th>Sofosbuvir/Velpatsvir</th>
<th>Sofosbuvir/Ledipasvir</th>
<th>Dacaltasvir + Sofosbuvir</th>
<th>Paritaprevir/r/Ombitasvir + Dasabuvir</th>
</tr>
</thead>
<tbody>
<tr>
<td>STRIBILD</td>
<td>↑ELB ↑GRAZ</td>
<td>↑TDF</td>
<td>↑TDF</td>
<td>↑DAC (Use 30 mg)</td>
<td>↑RIT ↑Cobi</td>
</tr>
<tr>
<td>GENVOYA</td>
<td>↑ELB ↑GRAZ</td>
<td></td>
<td></td>
<td>↑DAC (Use 30 mg)</td>
<td>↑RIT ↑Cobi</td>
</tr>
<tr>
<td>DOL or RAL + TRUVADA</td>
<td>↑TDF</td>
<td>↑TDF</td>
<td></td>
<td>Use DAC 60 mg</td>
<td>↑DOL ↑DAS</td>
</tr>
<tr>
<td>TRIUMEQ</td>
<td>↑TDF</td>
<td></td>
<td></td>
<td></td>
<td>↑DOL ↑DAS</td>
</tr>
<tr>
<td>COMPLERA</td>
<td>↑TDF</td>
<td>↑TDF</td>
<td></td>
<td>Use DAC 60 mg</td>
<td>↑RIL (↑QT)</td>
</tr>
<tr>
<td>ODEFSEY</td>
<td></td>
<td></td>
<td></td>
<td>Use DAC 60 mg</td>
<td>↑RIL (↑QT)</td>
</tr>
<tr>
<td>ATRIPLA</td>
<td>↓ELB ↓GRAZ</td>
<td>↓VEL</td>
<td>↑TDF</td>
<td>Use DAC 60 mg</td>
<td></td>
</tr>
<tr>
<td>DRV/r + TRUVADA</td>
<td>↑GRAZ</td>
<td>↑TDF</td>
<td>↑TDF</td>
<td>Use DAC 60 mg</td>
<td>↓DRV (no am RIT)</td>
</tr>
<tr>
<td>ATZ/r + TRUVADA</td>
<td>↑GRAZ</td>
<td>↑TDF</td>
<td>↑TDF</td>
<td>Use DAC 60 mg</td>
<td>↑PAR (no am RIT)</td>
</tr>
</tbody>
</table>

Shading: Green=OK to co-administer; Yellow=use caution; Red=avoid use

# Drug-Drug Interactions Between HCV Antivirals and Other Drugs

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Elbasvir/Grazoprevir</th>
<th>Sofosbuvir/Velpatsvir</th>
<th>Sofosbuvir/Ledipasvir</th>
<th>Dacaltasvir + Sofosbuvir</th>
<th>Paritaprevir/r/Ombitasvir + Dasabuvir</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Statins</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atorvastatin</td>
<td>Max: 20 mg/d</td>
<td>Monitor</td>
<td></td>
<td></td>
<td>↑ statin; Avoid</td>
</tr>
<tr>
<td>Lovastatin</td>
<td>Monitor</td>
<td></td>
<td></td>
<td></td>
<td>↑ statin; Avoid</td>
</tr>
<tr>
<td>Simvastatin</td>
<td>Monitor</td>
<td></td>
<td></td>
<td></td>
<td>↑ statin; Avoid</td>
</tr>
<tr>
<td>Rosuvastatin</td>
<td>Max: 10 mg/d</td>
<td>Max: 10 mg/d</td>
<td>↑ statin; Avoid</td>
<td></td>
<td>Max: 10 mg/d</td>
</tr>
<tr>
<td>Pravastatin</td>
<td>Monitor</td>
<td></td>
<td></td>
<td></td>
<td>Max: 40 mg/d</td>
</tr>
<tr>
<td><strong>Methadone</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Proton pump inhibitors</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>↓ PPI</td>
</tr>
<tr>
<td>Take DAA w/ food 4 hrs before PPI; Max: omeprazole 20 mg/d or equivalent</td>
<td>Take DAA w/ food 4 hrs before PPI; Max: omeprazole 20 mg/d or equivalent</td>
<td>Take DAA w/ food 4 hrs before PPI; Max: omeprazole 20 mg/d or equivalent</td>
<td>▼ omeprazole 40 mg/d or equivalent</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Case 1: 54 yo Woman with HIV and Genotype 1a Chronic HCV

- Discussed care with care providers
  - Changed ART: dolutegravir + tenofovir/emtricitabine
  - Confirmed omeprazole 20 mg/day

- 4 weeks later:
  - No complaints on new regimen
  - Tolerating without adverse effects
  - HIV RNA 0 copies/mL
Question:
How Would You Treat This Patient?

A. Initiate sofosbuvir/velpatasvir x 24 weeks
B. Initiate sofosbuvir/ledipasvir x 12 weeks
C. Initiate elbasvir/grazoprevir x 12 weeks
D. Initiate sofosbuvir + ribavirin x 24 weeks
How Would You Treat This Patient?

- Initiate sofosbuvir/velpatasvir x 24 weeks: 0%
- Initiate sofosbuvir/ledipasvir x 12 weeks: 0%
- Initiate elbasvir/grazoprevir x 12 weeks: 0%
- Initiate sofosbuvir + ribavirin x 24 weeks: 0%

Source: https://api.event.com/colling/v1/api/polls/sp35vtrg
Goals of Antiviral Therapy

- Eliminate Virus
- Prevent/Reduce Liver Fibrosis
- Prevent Complications
- Viral Cure (SVR12)*
- Delay Cirrhosis
- Prevent HCC, Extrahepatic Dz, HCV Transmission

* SVR = Sustained virologic response (no HCV RNA ≥12 wks after end of therapy)
Direct-Acting Antivirals (DAAs)
Target Specific HCV Proteins

Structural
- Capsid shell
  - Core
- Envelope glycoproteins
  - E1
  - E2

Non-Structural
- Viral assembly
  - P7
- Protease
  - NS2
- Serine Protease
- Membranous web formation
- Viral replication or assembly
- RNA dependent RNA polymerase
  - NS3
  - NS4A
  - NS4B
  - NS5A
  - NS5B
Direct-Acting Antivirals (DAAs) Target Specific HCV Proteins

**Structural**
- Core
- E1
- E2

**Non-Structural**
- P7
- NS2
- NS3
- NS4A
- NS4B
- NS5A
- NS5B

**NS3/4A Protease Inhibitors**
- 1\textsuperscript{st}: Boceprevir, telaprevir
- 2\textsuperscript{nd}: Simeprevir, paritaprevir, grazoprevir
- Low-intermediate barrier to resistance
- Narrow genotypic coverage
Direct-Acting Antivirals (DAAs) Target Specific HCV Proteins

**Structural**
- Core
- E1
- E2

**Non-Structural**
- P7
- NS2
- NS3
- NS4A
- NS4B
- NS5A
- NS5B

**NS5A Inhibitors**
- 1\textsuperscript{st}: Ledipasvir, ombitasvir, daclatasvir
- 2\textsuperscript{nd}: Elbasvir, velpatasvir
- Intermediate barrier to resistance
- Multi-genotypic coverage
Direct-Acting Antivirals (DAAs)
Target Specific HCV Proteins

### Structural
- Core
- E1
- E2

### Non-Structural
- P7
- NS2
- NS3
- NS4A
- NS4B
- NS5A
- NS5B

#### NS5B Polymerase Inhibitors
- **Nucleos(t)ide Analogues**
  - Sofosbuvir
  - High barrier to resistance
  - Pan-genotypic coverage

- **Non-Nucleoside Analogues**
  - Dasabuvir
  - Low barrier to resistance
  - Limited genotypic coverage

#### Targets
- Capsid shell
- Envelope glycoproteins
- Viral assembly
- Protease
- Serine Protease
- Membranous web formation
- Viral replication or assembly
- RNA dependent RNA polymerase
 Currently Available DAAs Target Specific HCV Proteins

<table>
<thead>
<tr>
<th>Direct-Acting Antiviral</th>
<th>Trade Name</th>
<th>Drug Classes</th>
<th>HCV Genotype Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sofosbuvir</td>
<td>Sovaldi</td>
<td>NS5B inhibitor</td>
<td>Pan-genotypic</td>
</tr>
<tr>
<td>Simeprevir</td>
<td>Olysio</td>
<td>NS3/4A inhibitor</td>
<td>GT 1, 2, 4, 5, 6</td>
</tr>
<tr>
<td>Sofosbuvir/Ledipasvir</td>
<td>Harvoni</td>
<td>NS5A + NS5B inhibitors</td>
<td>GT 1</td>
</tr>
<tr>
<td>Paritaprevir/r/Ombitasvir</td>
<td>Technivie</td>
<td>NS3A + NS5A inhibitors</td>
<td>GT 4</td>
</tr>
<tr>
<td>Daclatasvir</td>
<td>Daklinza</td>
<td>NS5A inhibitor</td>
<td>Pan-genotypic</td>
</tr>
<tr>
<td>Elbasvir/Grazoprevir</td>
<td>Zepatier</td>
<td>NS3A, NS5A inhibitors</td>
<td>GT 1, 4</td>
</tr>
<tr>
<td>Sofosbuvir/Velpatasvir</td>
<td>Epclusa</td>
<td>NS5A + NS5B inhibitors</td>
<td>Pan-genotypic</td>
</tr>
<tr>
<td>Paritaprevir/r/Ombitasvir + Dasabuvir</td>
<td>Viekira XR</td>
<td>PI + NS5A + NS5B inhibitors</td>
<td>GT 1</td>
</tr>
</tbody>
</table>

r=ritonavir
www.hcvguidelines.org
### HCV Genotype 1 Regimens (2017): HCV Treatment-Naïve

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Duration of Therapy (Weeks)</th>
<th>Genotype 1a</th>
<th>Genotype 1b</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No Cirrhosis</td>
<td>Cirrhosis</td>
<td>No Cirrhosis</td>
</tr>
<tr>
<td>Elbasvir/grazoprevir</td>
<td>12 (16+RBV)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>12 (16+RBV)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>12</td>
</tr>
<tr>
<td>Sofosbuvir/velpatasvir</td>
<td>12</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>Sofosbuvir/ledipasvir</td>
<td>12&lt;sup&gt;b&lt;/sup&gt;</td>
<td>12</td>
<td>12&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Daclatasvir + Sofosbuvir</td>
<td>12</td>
<td>24</td>
<td>12</td>
</tr>
<tr>
<td>Paritaprevir/r/ombitasvir + Dasabuvir</td>
<td>12 (with RBV)</td>
<td>24 (with RBV)</td>
<td>12</td>
</tr>
</tbody>
</table>

<sup>a</sup> NS5A resistance-associated substitutions (RAS) detected

<sup>b</sup> 8 weeks if HCV RNA <6 million IU/mL, treatment-naïve, no cirrhosis, no HIV

RBV = ribavirin

www.hcvguidelines.org
NS5A Resistance Testing

- Perform in GT 1a patients prior to treatment with elbasvir/grazoprevir

- Commercially available test

- Identifies high-fold change HCV RAS for elbasvir
  - At amino acid positions M28, Q30, L31, Y93
  - Prevalence of RAS at any of these positions = 12%

- Presence of one or more of these RAS:
  - Add ribavirin, ↑ treatment duration to 16 weeks
## HCV Genotype 1 Regimens (2017): HCV Treatment-Naïve

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<td>12 (16+RBV)(^a)</td>
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<td>12</td>
</tr>
<tr>
<td>Sofosbuvir/velpatasvir</td>
<td>12</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>Sofosbuvir/ledipasvir</td>
<td>12(^b)</td>
<td>12</td>
<td>12(^b)</td>
</tr>
<tr>
<td>Daclatasvir + Sofosbuvir</td>
<td>12</td>
<td>24</td>
<td>12</td>
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<td>Paritaprevir/r/ombitasvir + Dasabuvir</td>
<td>12 (with RBV)</td>
<td>24 (with RBV)</td>
<td>12</td>
</tr>
</tbody>
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\(^a\) NS5A resistance-associated substitutions (RAS) detected  
\(^b\) 8 weeks if HCV RNA <6 million IU/mL, treatment-naïve, no cirrhosis, no HIV  

RBV = ribavirin  

www.hcvguidelines.org
# HCV Genotypes 2-6 Regimens (2017): HCV Treatment-Naïve

<table>
<thead>
<tr>
<th>GT</th>
<th>Treatment Regimens</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>Sofosbuvir/velpatasvir x 12 wks</td>
</tr>
<tr>
<td></td>
<td>Daclatasvir + Sofosbuvir x 12 wks (16-24 wks if cirrhotic)</td>
</tr>
<tr>
<td>3</td>
<td>Sofosbuvir/velpatasvir x 12 wks</td>
</tr>
<tr>
<td></td>
<td>Daclatasvir + Sofosbuvir x 12 wks (24 wks ± RBV if cirrhotic)</td>
</tr>
<tr>
<td>4</td>
<td>Sofosbuvir/velpatasvir x 12 wks</td>
</tr>
<tr>
<td></td>
<td>Sofosbuvir/ledipasvir x 12 wks</td>
</tr>
<tr>
<td></td>
<td>Elbasvir/grazoprevir x 12 wks</td>
</tr>
<tr>
<td></td>
<td>Paritaprevir/r/ombitasvir + RBV x 12 wks</td>
</tr>
<tr>
<td>5 or 6</td>
<td>Sofosbuvir/velpatasvir x 12 wks</td>
</tr>
<tr>
<td></td>
<td>Sofosbuvir/ledipasvir x 12 wks</td>
</tr>
</tbody>
</table>

GT=genotype; RBV=ribavirin
www.hcvguidelines.org
HCV Cure Rates Comparable in HIV/HCV and HCV Only Patients

<table>
<thead>
<tr>
<th>DAA Regimen (12 Weeks, Once Daily)</th>
<th>Treatment-Naïve Genotype 1 Sustained Virologic Response (SVR12)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HIV/HCV-Coinfected</td>
</tr>
<tr>
<td>Sofosbuvir/Ledipasvir</td>
<td>95%</td>
</tr>
<tr>
<td>Paritaprevir/r/Ombitasvir + Dasabuvir</td>
<td>94%</td>
</tr>
<tr>
<td>Elbasvir/Grazoprevir</td>
<td>96%</td>
</tr>
<tr>
<td>Sofosbuvir/Velpatasvir</td>
<td>95%</td>
</tr>
</tbody>
</table>

www.hcvguidelines.org
Sustained Virologic Response (SVR) Reduces Mortality in HCV

530 patients followed median 8.4 years after interferon treatment
SVR=HCV RNA(−) ≥24 weeks (now ≥12 weeks) after stopping therapy

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Cumulative Incidence at 10 Years</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>SVR</td>
<td>No SVR</td>
<td></td>
</tr>
<tr>
<td>Liver-related mortality or liver transplant</td>
<td>1.9%</td>
<td>27.4%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>All-cause mortality</td>
<td>8.9%</td>
<td>26.0%</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Van der Meer AJ. JAMA 2012:308:2584-93.
Question: What are your treatment options?

A. Initiate sofosbuvir/velpatasvir x 24 weeks
B. Initiate sofosbuvir/ledipasvir x 12 weeks
C. Initiate elbasvir/grazoprevir x 12 weeks
D. Initiate sofosbuvir + ribavirin x 24 weeks
What are your treatment options?

- Initiate sofosbuvir/velpatasvir x 24 weeks: 0%
- Initiate sofosbuvir/ledipasvir x 12 weeks: 0%
- Initiate elbasvir/grazoprevir x 12 weeks: 0%
- Initiate sofosbuvir + ribavirin x 24 weeks: 0%
## HCV Genotype 1 Regimens (2017): HCV Treatment-Naïve

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Duration of Therapy (Weeks)</th>
<th>Genotype 1a</th>
<th>Genotype 1b</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>No Cirrhosis</td>
<td>Cirrhosis</td>
</tr>
<tr>
<td>Elbasvir/grazoprevir</td>
<td>12 (16+RBV)(^a)</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>Sofosbuvir/velpatasvir</td>
<td>12</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>Sofosbuvir/ledipasvir</td>
<td>12(^b)</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>Daclatasvir + Sofosbuvir</td>
<td>12</td>
<td>24</td>
<td>12</td>
</tr>
<tr>
<td>Paritaprevir/r/ombitasvir + Dasabuvir</td>
<td>12 (with RBV)</td>
<td>24</td>
<td>12</td>
</tr>
</tbody>
</table>

\(^a\) NS5A resistance-associated substitutions (RAS) detected

\(^b\) 8 weeks if HCV RNA <6 million IU/mL, treatment-naïve, no cirrhosis, no HIV

RBV = ribavirin

[www.hcvguidelines.org](http://www.hcvguidelines.org)
# HCV Genotype 1 Regimens (2017): HCV Treatment-Naïve

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Duration of Therapy (Weeks)</th>
<th>Genotype 1a</th>
<th>Genotype 1b</th>
<th>Genotype 1b (with RBV)</th>
<th>Genotype 1b (with RBV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elbasvir/grazoprevir</td>
<td></td>
<td>12</td>
<td>12</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>Sofosbuvir/velpatasvir</td>
<td></td>
<td>12</td>
<td>12</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>Sofosbuvir/ledipasvir</td>
<td></td>
<td>12&lt;sup&gt;b&lt;/sup&gt;</td>
<td>12</td>
<td>12&lt;sup&gt;b&lt;/sup&gt;</td>
<td>12</td>
</tr>
<tr>
<td>Daclatasvir + Sofosbuvir</td>
<td></td>
<td>12</td>
<td>24</td>
<td>12</td>
<td>24</td>
</tr>
<tr>
<td>Paritaprevir/r/ombitasvir + Dasabuvir</td>
<td></td>
<td>12&lt;sup&gt;a&lt;/sup&gt; (with RBV)</td>
<td>24&lt;sup&gt;a&lt;/sup&gt; (with RBV)</td>
<td>12</td>
<td>12</td>
</tr>
</tbody>
</table>

<sup>a</sup> NS5A resistance-associated substitutions (RAS) detected

<sup>b</sup> 8 weeks if HCV RNA <6 million IU/mL, treatment-naïve, no cirrhosis, no HIV

RBV = ribavirin

Use requires antecedent NS5A resistance testing!
### HCV Genotype 1 Regimens (2017): HCV Treatment-Naïve

<table>
<thead>
<tr>
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<th>Duration of Therapy (Weeks)</th>
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<th>Genotype 1b</th>
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<td></td>
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<td>Cirrhosis</td>
</tr>
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<td><strong>Elbasvir/grazoprevir</strong></td>
<td></td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>(16+RBV)&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Sofosbuvir/velpatasvir</strong></td>
<td></td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td><strong>Sofosbuvir/ledipasvir</strong></td>
<td></td>
<td>12&lt;sup&gt;b&lt;/sup&gt;</td>
<td>12</td>
</tr>
<tr>
<td><strong>Daclatasvir + Sofosbuvir</strong></td>
<td></td>
<td>12</td>
<td>24</td>
</tr>
<tr>
<td><strong>Paritaprevir/r/ombitasvir + Dasabuvir</strong></td>
<td></td>
<td>12&lt;sup&gt;RBV&lt;/sup&gt;</td>
<td>24&lt;sup&gt;RBV&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup> NS5A resistance-associated substitutions (RAS) detected

<sup>b</sup> 8 weeks if HCV RNA < 6 million IU/mL, treatment-naïve, no cirrhosis, no HIV

**RBV** = ribavirin
### HCV Genotype 1 Regimens (2017): HCV Treatment-Naïve

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Duration of Therapy (Weeks)</th>
<th>Genotype 1a No Cirrhosis</th>
<th>Genotype 1a Cirrhosis</th>
<th>Genotype 1b No Cirrhosis</th>
<th>Genotype 1b Cirrhosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elbasvir/grazoprevir</td>
<td></td>
<td>12 (16+RBV)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>12 (16+RBV)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>Sofosbuvir/velpatasvir</td>
<td></td>
<td>12</td>
<td>12</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td><strong>Sofosbuvir/ledipasvir</strong></td>
<td></td>
<td>12&lt;sup&gt;b&lt;/sup&gt;</td>
<td>12</td>
<td>12&lt;sup&gt;b&lt;/sup&gt;</td>
<td>12</td>
</tr>
<tr>
<td>Daclatasvir + Sofosbuvir</td>
<td></td>
<td>12</td>
<td>24</td>
<td>12</td>
<td>24</td>
</tr>
<tr>
<td>Paritaprevir/r/ombitasvir + Dasabuvir</td>
<td></td>
<td>12 (with RBV)</td>
<td>24 (with RBV)</td>
<td>12</td>
<td>12</td>
</tr>
</tbody>
</table>

<sup>a</sup> NS5A resistance-associated substitutions (RAS) detected

<sup>b</sup> 8 weeks if HCV RNA <6 million IU/mL, treatment-naïve, no cirrhosis, no HIV

RBV = ribavirin
Case 1: 54 yo Woman with HIV and Genotype 1a Chronic HCV

- Initiated HCV therapy in 3/2016
  - Sofosbuvir/ledipasvir once daily x 12 weeks
- Week 4 of HCV therapy:
  - Missed 2-3 treatment doses
  - HCV RNA <43 IU/mL (detectable); ALT 23
- Week 8 of HCV therapy: HCV RNA 0 IU/mL
Case 1: 54 yo Woman with HIV and Genotype 1a Chronic HCV

- Week 12 of HCV therapy: HCV RNA 0 IU/mL
  - CD4+ 662/mm³ (26%); HIV 0 copies/mL
- 4 weeks after end of HCV treatment:
  - HCV RNA 0 IU/mL
- 12 weeks after end of HCV treatment:
  - HCV RNA 0 IU/mL (achieved SVR = viral cure)
Risk of HCV Reinfection and HCC After SVR

• Estimated incidence rates of HCV reinfection:
  – Persons who inject drugs: 6/100 person-years
  – Men who have sex with men: 15/100 person-years

• HCC incidence after SVR (cirrhosis): 0.3%/year

• Need for surveillance, education

Case 2: 63 yo Man with HIV and Genotype 3a Chronic HCV

- HIV (4/1999):
  - Risk factors: unprotected sex, IV drug use
  - Efavirenz/tenofovir (TDF)/emtricitabine (2009)
  - 6/2016: CD4 468/mm$^3$ (28%); HIV 0 copies/mL

- HCV antibody-positive (9/2002):
  - HCV genotype 3a; HCV RNA 5.4 log IU/mL
  - HCV treatment-naïve
Case 2: 63 yo Man with HIV and Genotype 3a Chronic HCV

- Past History: hypertension
- Medications:
  - Efavirenz/tenofovir (TDF)/emtricitabine
  - Amlodipine
- Social History:
  - IV heroin, intranasal cocaine (1965-1998)
  - Denies alcohol, tobacco
Case 2: 63 yo Man with HIV and Genotype 3a Chronic HCV

- Physical exam: BMI 24.6 kg/m^2
  - No hepatomegaly, stigmata of liver disease
- Laboratory data:
  - TB 0.7; Alb 4.2; INR 0.9; ALT 53; AST 42
  - WBC 5.2; Hgb 14.7; platelets 153; Cr=0.91
- Elastography: 13.3 kPA (F4) $\rightarrow$ cirrhosis
- Liver U/S (-) masses, ascites; EGD (-) varices
Question: What Would You Do?

A. Initiate sofosbuvir/velpatasvir x 12 weeks
B. Initiate daclatasvir + sofosbuvir x 12 weeks
C. Modify ART regimen
D. Modify anti-hypertensive treatment
What would you do?

- Initiate sofosbuvir/velpatasvir x 12 weeks: 0%
- Initiate daclatasvir + sofosbuvir x 12 weeks: 0%
- Modify ART regimen: 0%
- Modify anti-hypertensive treatment: 0%

Source:
https://api-event.com/polling/41/api/polls/evvw10k
## HCV Genotype 3 Regimens (2017): HCV Treatment-Naïve

<table>
<thead>
<tr>
<th>GT</th>
<th>Treatment Regimens</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>Sofosbuvir/velpatasvir x 12 wks</td>
</tr>
<tr>
<td></td>
<td>Daclatasvir + Sofosbuvir x 12 wks (16-24 wks if cirrhotic)</td>
</tr>
<tr>
<td>3</td>
<td>Sofosbuvir/velpatasvir x 12 wks</td>
</tr>
<tr>
<td></td>
<td>Daclatasvir + Sofosbuvir x 12 wks (24 wks ± RBV if cirrhotic)</td>
</tr>
<tr>
<td>4</td>
<td>Sofosbuvir/velpatasvir x 12 wks</td>
</tr>
<tr>
<td></td>
<td>Sofosbuvir/ledipasvir x 12 wks</td>
</tr>
<tr>
<td></td>
<td>Elbasvir/grazoprevir x 12 wks</td>
</tr>
<tr>
<td></td>
<td>Paritaprevir/r/ombitasvir + RBV x 12 wks</td>
</tr>
<tr>
<td>5 or 6</td>
<td>Sofosbuvir/velpatasvir x 12 wks</td>
</tr>
<tr>
<td></td>
<td>Sofosbuvir/ledipasvir x 12 wks</td>
</tr>
</tbody>
</table>

GT=genotype; RBV=ribavirin

www.hcvguidelines.org
Case 2: 63 yo Man with HIV and Genotype 3a Chronic HCV

- Past History: hypertension
- Medications:
  - Efavirenz/tenofovir (TDF)/emtricitabine
  - Amlodipine
- Social History:
  - IV heroin, intranasal cocaine (1965-1998)
  - Denies alcohol, tobacco
## Antiretroviral-DAA Drug-Drug Interactions

<table>
<thead>
<tr>
<th>ARV</th>
<th>Elbasvir/Grazoprevir</th>
<th>Sofosbuvir/Velpatsvir</th>
<th>Sofosbuvir/Ledipasvir</th>
<th>Dacaltasvir + Sofosbuvir</th>
<th>Paritaprevir/r/ Ombitasvir + Dasabuvir</th>
</tr>
</thead>
<tbody>
<tr>
<td>STRIBILD</td>
<td>↑ELB ↑GRAZ</td>
<td>↑TDF</td>
<td>↑TDF</td>
<td>↑DAC (Use 30 mg)</td>
<td>↑RIT ↑Cobi</td>
</tr>
<tr>
<td>GENVOYA</td>
<td>↑ELB ↑GRAZ</td>
<td></td>
<td></td>
<td>↑DAC (Use 30 mg)</td>
<td>↑RIT ↑Cobi</td>
</tr>
<tr>
<td>DOL or RAL + TRUVADA</td>
<td>↑TDF</td>
<td>↑TDF</td>
<td></td>
<td>Use DAC 60 mg</td>
<td>↑DOL ↑DAS</td>
</tr>
<tr>
<td>TRIUMEQ</td>
<td></td>
<td></td>
<td>↑TDF</td>
<td>Use DAC 60 mg</td>
<td>↑DOL ↑DAS</td>
</tr>
<tr>
<td>COMPLERA</td>
<td>↑TDF</td>
<td>↑TDF</td>
<td></td>
<td>Use DAC 60 mg</td>
<td>↑RIL (↑QT)</td>
</tr>
<tr>
<td>ODEFSEY</td>
<td></td>
<td></td>
<td>↑TDF</td>
<td>Use DAC 60 mg</td>
<td>↑RIL (↑QT)</td>
</tr>
<tr>
<td>ATRIPLA</td>
<td>↓ELB ↓GRAZ</td>
<td>↓VEL</td>
<td>↑TDF</td>
<td>Use DAC 60 mg</td>
<td></td>
</tr>
<tr>
<td>DRV/r + TRUVADA</td>
<td>↑GRAZ</td>
<td>↑TDF</td>
<td>↑TDF</td>
<td>Use DAC 60 mg</td>
<td>↓DRV (no am RIT)</td>
</tr>
<tr>
<td>ATZ/r + TRUVADA</td>
<td>↑GRAZ</td>
<td>↑TDF</td>
<td>↑TDF</td>
<td>Use DAC 60 mg</td>
<td>↑PAR (no am RIT)</td>
</tr>
</tbody>
</table>

Shading: Green=OK to co-administer; Yellow=use caution; Red=avoid use
Case 2: 63 yo Man with HIV and Genotype 3a Chronic HCV

- Discussed care with care provider
  - Changed ART: dolutegravir + TAF/emtricitabine

- 4 weeks later:
  - No adverse effects; HIV RNA 0 copies/mL

- Initiated sofosbuvir/velpatasvir x 12 weeks
  - HCV RNA 0 IU/mL at treatment end; Await SVR12
Case 3: 58 yo Man with HIV and GT 1a Chronic HCV on Dialysis

- HIV (6/2000):
  - Risk factor: IV drug use
  - Dolutegravir, abacavir, lamivudine
  - 11/2016: CD4 996/mm$^3$ (37%); HIV 0 copies/mL

- HCV antibody-positive (6/2000):
  - HCV genotype 1a; HCV RNA 6.0 log IU/mL
  - HCV treatment-naïve
Case 3: 58 yo Man with HIV and GT 1a Chronic HCV on Dialysis

- Past History:
  - Hypertension
  - Chronic kidney disease → dialysis

- Medications:
  - Dolutegravir, abacavir, lamivudine
  - Amlodipine, labetolol, metoprolol

- Social History: Remote IV heroin; no alcohol
Case 3: 58 yo Man with HIV and GT 1a Chronic HCV on Dialysis

- Physical exam:
  - Right upper arm AV graft
  - No hepatomegaly; no stigmata of liver disease

- Laboratory data:
  - TB 0.7; Alb 4.0; INR 1.0; ALT 14; AST 17
  - WBC 4.1; Hgb 10.6; platelets 258; Cr=8.7
  - HAV IgG (+); anti-HBs (+); NS5A RAS (-)

- Elastography: 9.4 kPA (F2)
Question: What Treatment Should We Recommend for This Patient?

A. Sofosbuvir/velpatasvir x 12 weeks
B. Paritaprevir/ritonavir/ombitasvir + dasabuvir + ribavirin 200 mg/d x 12 weeks
C. Sofosbuvir/ledipasvir x 12 weeks
D. Elbasvir/grazoprevir x 12 weeks
Insert Web Page

This app allows you to insert secure web pages starting with https:// into the slide deck. Non-secure web pages are not supported for security reasons.

Please enter the URL below.

https://api.cvent.com/polling/v1/api/polls/sp71fnnd

Note: Many popular websites allow secure access. Please click on the preview button to ensure the web page is accessible.
HCV Treatment With Mild-Moderate Renal Impairment (CrCl 30-80 mL/min)

- No dosage adjustment is necessary with:

<table>
<thead>
<tr>
<th>Regimen</th>
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<tbody>
<tr>
<td>Elbasvir/grazoprevir</td>
</tr>
<tr>
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<td>Sofosbuvir/ledipasvir</td>
</tr>
<tr>
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</tr>
<tr>
<td>Paritaprevir/r/ombitasvir + Dasabuvir</td>
</tr>
</tbody>
</table>

Creatinine clearance (CrCl) = \((140 - \text{age(yr)})*\text{weight(kg)})/\((72*\text{Cr(mg/dL)})\)*0.85 if female
# HCV Treatment With Severe Renal Impairment
(CrCL <30 mL/min or End-Stage Renal Disease)

<table>
<thead>
<tr>
<th>GT</th>
<th>Available Regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a</td>
<td>Elbasvir/grazoprevir x 12 wks <em>(Recommended)</em></td>
</tr>
<tr>
<td></td>
<td>Paritaprevir/r/ombitasvir + dasabuvir + RBV 200 mg daily x 12 wks <em>(Alternative)</em></td>
</tr>
<tr>
<td>1b</td>
<td>Elbasvir/grazoprevir x 12 wks</td>
</tr>
<tr>
<td></td>
<td>Paritaprevir/r/ombitasvir + dasabuvir x 12 wks</td>
</tr>
<tr>
<td>4</td>
<td>Elbasvir/grazoprevir x 12 wks</td>
</tr>
<tr>
<td>2, 3, 5, 6</td>
<td>PEG-IFN + RBV 200 mg daily x 48 wks</td>
</tr>
</tbody>
</table>

Creatinine clearance (CrCl) = \[\frac{[140 - \text{age(yr)}] \times \text{weight(kg)}}{[72 \times \text{Cr(mg/dL)}]} \times 0.85\] if female

GT=genotype; RBV=ribavirin

www.hcvguidelines.org
Question: What Treatment Should We Recommend for This Patient?

A. Sofosbuvir/velpatasvir x 12 weeks

B. Paritaprevir/ritonavir/ombitasvir + dasabuvir + ribavirin 200 mg/d x 12 weeks

C. Sofosbuvir/ledipasvir x 12 weeks

D. Elbasvir/grazoprevir x 12 weeks

Preferred
Take-Home Points

• Liver fibrosis stage: important pre-HCV therapy
  – Any method acceptable → just be sure to stage

• Consider drug-drug interactions with DAAs

• DAAs efficacious, well tolerated in HIV/HCV
  – Genotype, cirrhosis, renal disease influence choice

• SVR ↓ ESLD, mortality in HIV/HCV

• Important to educate regarding reinfection
ACTHIV 2017: A State-of-the-Science Conference for Frontline Health Professionals