Hepatitis C Infection: Pharmacotherapy Update

Autumn Bagwell, PharmD, BCPS, AAHIVP
Infectious Diseases Clinical Pharmacist
Vanderbilt Specialty Pharmacy
Disclosures

- I have no financial disclosures.
Objectives

- Describe and apply appropriate screening criteria for HCV
- Describe the general biology and life cycle of HCV
- Distinguish pharmacologic characteristics between HCV Direct Acting Antiviral classes
- Describe treatment strategies for patients with HCV infection
- Recognize common drug interactions with direct-acting antivirals (DAA)
Outline

- HCV epidemiology and biology
- HCV Treatment Considerations
- Currently Available Direct Acting Antivirals (DAA)
- DAA medication interactions
- Current HCV treatment regimens
- Special Populations
HCV Epidemiology

- 170 million infections worldwide
- 3.2 to 5.2 million infections in the US

HCV and Mortality in the USA

Acute Cases of Hepatitis C in Tennessee 2010-2014

Map Created by Viral Hepatitis Surveillance
Data Source: NBS, accessed June 2015
Method: Manual, 5 Classes
Map Created on: September 16, 2015
Note: 22 records were missing address information

Case Count
n=706

- 0
- 5 or Less
- 6 - 10
- 11 - 25
- 26 - 66
HCV Risk Factors

- Injection drug use: 60%
- Sexual: 15%
- Transfusion (before screening): 10%
- Other (hemodialysis; health care work; perinatal): 5%
- Unknown: 10%
HCV Screening

- One-time HCV testing recommended for persons born 1945-1965

<table>
<thead>
<tr>
<th>Risk behaviors</th>
<th>Risk exposure</th>
<th>Other</th>
</tr>
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<tbody>
<tr>
<td>Injection-drug use (current or ever)</td>
<td>Long-term hemodialysis (ever)</td>
<td>HIV infection</td>
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<tr>
<td>Intranasal illicit drug use</td>
<td>Getting a tattoo in an unregulated setting</td>
<td>Unexplained chronic liver disease</td>
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<td>Healthcare workers</td>
<td>Solid organ donors</td>
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<td>Children born to HCV-infected women</td>
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<tr>
<td></td>
<td>Prior recipients of transfusions or organ transplants</td>
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<tr>
<td></td>
<td>Ever incarcerated</td>
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</table>
HCV Diagnosis

- **HCV Antibody**
  - Tests for *exposure*
  - Near 100% sensitivity once >6 months after infection

- **HCV RNA Polymerase Chain Reaction (PCR)**
  - Tests for *active infection*
  - Helps determine treatment duration

- **HCV Genotype**
  - Defines treatment options
  - Adds prognostic info
AASLD/IDSA Guidelines

HCV antibody

Nonreactive

No HCV antibody detected

Stop*

Reactive

HCV RNA

Detected

Current HCV infection

Link to care

Not detected

No current HCV infection

Additional testing as appropriate†
HCV Infection

- Single-stranded RNA virus of the *Flaviviridae* family
- Predominantly infects liver cells
- Six major genotypes, further classified to subtypes
  - US: genotypes 1a and 1b most common
- Most patients are asymptomatic and undiagnosed

- Extrahepatic manifestations:
  - Cryoglobulinemia
  - B-cell non-Hodgkin’s lymphoma
  - Sjogren’s syndrome
  - Glomerulonephritis
  - Arthritis
  - Corneal ulcers
  - Thyroid disease
  - Neuropathies
  - Porphyria cutanea tarda
  - Insulin resistance
  - Chronic fatigue
Natural History of HCV

- Cirrhosis may take >20 years to develop in the absence of comorbidities
- Factors Impacting Rate of Progression of Fibrosis:
  - Older age
  - Male sex
  - HIV or HBV co-infection
  - Metabolic factors
  - Use of alcohol
  - Genotype 3 infection
Outline

- HCV epidemiology and biology
- **HCV Treatment Considerations**
- Currently Available Direct Acting Antivirals (DAA)
- DAA medication interactions
- Current HCV treatment regimens
- Special Populations
Goal of Treatment

- The goal of treatment of HCV-infected persons is to reduce all-cause mortality and liver-related health adverse consequences, including end-stage liver disease and hepatocellular carcinoma, by the achievement of virologic cure as evidenced by a sustained virologic response.

Rating: Class I, Level A
Primary Factors when Selecting HCV Treatment

1. Genotype
2. Degree of fibrosis
   - I.e. Non-cirrhotic vs. cirrhotic
3. Treatment history
   - I.e. Treatment naïve vs. treatment experienced
   - Recommendations may differ depending on what therapies were used previously (i.e. PEG-IFN vs. DAA-based therapy)
Secondary Factors when Selecting HCV Treatment

- **Efficacy**
  - Relatively equal among recommended regimens
- **Safety**
- **Side effect profile**
  - Including need for PEG-IFN or RBV
- **Drug-drug interactions**
- **Access**
  - **Cost**
  - **Formulary restrictions**
Recommendations for Testing, Managing, and Treating Hepatitis C

Released January 29, 2014
Last updated July 6th, 2016
Available at www.hcvguidelines.org
High Priority for Treatment Owing to High Risk for Complications

Fibrosis (Metavir F2)
Rating: Class I, level B

HIV-1 coinfection
Rating: Class I, Level A

Hepatitis B virus infection
Rating: Class IIa, Level B

Other coexistent liver disease
Rating: Class IIa, Level C

Debilitating fatigue
Rating: Class IIa, Level C

Type 2 Diabetes Mellitus (uncontrolled)
Rating: Class IIa, Level C

Porphyria cutanea tarda
Rating: Class IIb, Level C
Recommendations for When and in Whom to Initiate Treatment

- Treatment is recommended for all patients with chronic HCV infection, except those with short life expectancies that cannot be remediated by treating HCV, by transplantation, or by other directed therapy. Patients with short life expectancies owing to liver disease should be managed in consultation with an expert.

Rating: Class I, Level A
Benefits of Treatment

Liver failure

- Without SVR
- With SVR

Hepatocellular carcinoma

- Without SVR
- With SVR

Liver-related mortality or liver transplantation

- Without SVR
- With SVR

All-cause mortality

- Without SVR
- With SVR
Treatment Response in DAA Era

HCV Mono-infection SVR

- IFN
- pegIFN
- IFN+RBV
- P/R
- TPV/BOC+P/R
- DAA+P/R
- DAA+/-RBV

Modified slide courtesy of Susanna Naggie, MD and Cody Chastain, MD.
Outline

- HCV epidemiology and biology
- HCV Treatment Considerations
- Currently Available Direct Acting Antivirals (DAA)
- DAA medication interactions
- Current HCV treatment regimens
HCV Treatment Timeline

**Pre-2011**
- Peg-IFN
- RBV
- Telaprevir (Incevik®)
- Boceprevir (Victrelis®)

**July 2011**
- Peg-IFN
- RBV
- Telaprevir
- Boceprevir
- Simeprevir (Olysio®)
- Sofosbuvir (Sovaldi®)

**Nov-Dec 2013**
- Peg-IFN
- RBV
- Telaprevir
- Boceprevir
- Simeprevir
- Sofosbuvir
- (Harvoni®)
- ledipasvir, sofosbuvir
- (Viekira Pak®): parataprevir, ombitasvir, dasabuvir

**Oct-Dec 2014**
- Peg-IFN
- RBV
- Telaprevir
- Boceprevir
- Simeprevir
- Sofosbuvir
- (Harvoni®)
- ledipasvir, sofosbuvir
- (Viekira Pak®): parataprevir, ombitasvir, dasabuvir
- Daclatasvir (Daklinza®)

**July 2015**
- Peg-IFN
- RBV
- Simeprevir
- Sofosbuvir
- Ledipasvir
- Parataprevir
- Ombitasvir
- Dasabuvir
- Daclatasvir
- (Zepatier®): elbasvir, grazoprevir
- (Epclusa®): velpatasvir, Sofosbuvir

**Jan-June 2016**
- Peg-IFN
- RBV
- Sofosbuvir
- Ledipasvir
- Parataprevir
- Ombitasvir
- Dasabuvir
- Daclatasvir
- Velpatasvir, Sofosbuvir
HCV Replication Complex
HCV Therapies by Class

Nonspecific Antivirals
- Pegylated interferon-alfa
- Ribavirin

NS5B Polymerase Inhibitors (-buvir)
- Sofosbuvir
- Dasabuvir

NS3/4A Protease Inhibitors (-previr)
- Telaprevir
- Boceprevir
- Simeprevir
- Paritaprevir
- Grazoprevir
- Glecaprevir

NS5A Inhibitors (-asvir)
- Ledipasvir
- Ombitasvir
- Daclatasvir
- Elbasvir
- Velpatasvir
- Pibrentasvir
NS3/4A Protease Inhibitors

- *previr*
- Single tablet regimen
  - Simeprevir (Olysio®)
- Combination tablet regimens
  - Paritaprevir (Viekira Pak®)(Viekira XR®) (Technivie®)
  - Grazoprevir (Zepatier®)
  - Glecaprevir
Simeprevir (SMV; Olysio®)

- FDA approved on 11/22/13
- Indication in combination with sofosbuvir:
  - Genotype 1 and 4
  - Compensated cirrhosis
  - HIV/HCV coinfection
- Dosing: 1 capsule (150mg) daily with food
  - No renal dose adjustment
Simeprevir

- **Adverse effects:**
  - Rash, pruritus, nausea, photosensitivity, headache, fatigue, diarrhea, dizziness

- **Warnings/Precautions**
  - Not recommended in moderate or severe hepatic impairment (Child-Turcotte Pugh (CTP) Class B/C)
  - Sulfonamide moiety
  - Negatively impacted by GT 1a NS3/4A protease polymorphisms (Q80K)
  - Baseline HCV resistance testing is recommended
Simeprevir Drug Interactions

- Avoid strong CYP3A4 inhibitors
- Avoid strong CYP3A4 inducers
- Contraindicated HIV medications
  - All HIV protease inhibitors
  - Non-Nucleoside Reverse Transcriptase Inhibitors: efavirenz, etravirine, nevirapine
- Rosuvastatin: max dose 10mg
NS5B Polymerase Inhibitors

- **-buvir**
- Single tablet regimen
  - Sofosbuvir (Sovaldi®)
- Combination tablet regimens
  - Dasabuvir (Viekira Pak®) (Viekira XR®)
Sofosbuvir (SOF; Sovaldi®)

- FDA approved on 12/6/13
- Coformulated with:
  - Ledipasvir (Harvoni®)
  - Velpatasvir (Epclusa®)
- Indication (as Sovaldi® with ribavirin):
  - Genotypes 1-6
- Dosing: 1 tablet (400mg) daily with or without food

Sofosbuvir

- **Adverse effects:** (all ≤10%)
  - Fatigue, headache

- **Warnings/Precautions:**
  - Not recommended with severe renal impairment (GFR <30 ml/min/1.73m²)

- **Drug interactions:**
  - Substrate of P-gp and BCRP
  - Contraindicated with amiodarone
NS5A Protein Inhibitors

- *-asvir
- Single tablet regimen
  - Daclatasvir (Daklinza®)
- Combination tablet regimens
  - Ombitasvir (Viekira Pak®)(Viekira XR®) (Technivie®)
  - Ledipasvir (Harvoni®)
  - Velpatasvir (Epclusa®)
  - Elbasvir (Zepatier®)
  - Pibrentasvir
Daclatasvir (DCV; Daklinza®)

- FDA approved on 7/24/15
- Indication (in combination with sofosbuvir):
  - Genotypes 1 and 3
  - Compensated cirrhosis
  - Decompensated cirrhosis
  - Transplant recipients
Daclatasvir

- **Dosing:** 1 tablet daily with or without food
  - Typically 60mg daily
  - **Dose modification required:**
    - 30mg with strong CYP3A4 inhibitors
    - 90mg with moderate CYP3A4 inducers
    - Contraindicated with strong CYP3A inducers

- **No dose adjustment for renal impairment**
  - However, used with sofosbuvir which should be avoided in CrCl <30ml/min

http://www.hepatitis.uw.edu
Ledipasvir/Sofosbuvir (LDV/SOF; Harvoni®)

- FDA approved on 10/10/14

- Indications:
  - Genotypes 1, 4, 5, 6
  - Liver transplant patients with or without compensated cirrhosis (GT 1, 4)
  - Decompensated cirrhosis (GT 1)
  - HIV/HCV coinfection

- Dosing: LDV 90mg/SOF 400mg tablet daily with or without food

Ledipasvir/Sofosbuvir

- **Adverse effects:**
  - Fatigue, headache, nausea

- **Warnings/Precautions:**
  - Not recommended with severe renal impairment (GFR <30 ml/min/1.73m²)

- **Drug interactions:**
  - Acid reducing agents***
  - Contraindicated with amiodarone
Ombitasvir (OBV)/Paritaprevir (PTV)/ Ritonavir (RTV) +/- Dasabuvir (DBV)
(Viekira Pak®, Viekira XR®, Technivie®)

- Paritaprevir (PTV)
  - Class: NS3/4A protease inhibitor coformulated with ritonavir (RTV or /r)
- Ombitasvir (OBV)
  - Class: NS5A replication complex inhibitor
- Dasabuvir (DBV)
  - Class: NS5B RNA non-nucleoside polymerase inhibitor
Ombitasvir (OBV)/Paritaprevir (PTV)/ Ritonavir (RTV) +/- Dasabuvir (DBV)

- **Indications:**
  - Genotype 1
    - RBV used for HCV GT 1A
  - Liver transplant recipients with \( \leq \)F2 fibrosis
  - HIV/HCV coinfection
  - OBV/PTVr/DBV: Genotype 4

- **Dosing:**
  - Viekira Pak: 3 tablets in the morning and 1 tablet in the evening
  - Viekira XR: 3 tablets once daily
  - Technivie: 2 tablets daily with food
  - With food
  - No dose adjustment with renal dysfunction
Ombitasvir (OBV)/Paritaprevir (PTV)/ Ritonavir (RTV) +/- Dasabuvir (DBV)

- **Adverse effects:**
  - Fatigue, nausea, pruritus, insomnia, asthenia, skin reactions

- **Warnings/Precautions:**
  - Not recommended in moderate/severe hepatic impairment (CTP Class B/C)

- **Drug Interactions**
  - Avoid concomitant ethinyl estradiol therapy
  - Contraindicated with many drugs due to strong CYP3A inhibition by ritonavir
Elbasvir/Grazoprevir (EBV/GZP; Zepatier®)

- FDA approved on 1/28/16
- Class
  - Elbasvir
    - NS5A replication complex inhibitor
  - Grazoprevir
    - NS3/4A protease inhibitor
- Indications:
  - Genotypes 1 and 4
  - Renal impairment including those on hemodialysis (HD)
  - HIV/HCV coinfection
- Dosing: 1 tablet (EBV 50MG/GZR 100mg) daily with or without food
  - No dose adjustment for renal dysfunction
- Requires baseline NS5A resistance testing in genotype 1a
Elbasvir/Grazoprevir

- **Adverse effects:**
  - Fatigue, headache, nausea

- **Warnings/Precautions**
  - Not recommended in moderate/severe hepatic impairment (CTP Class B/C)
  - ALT elevations: Monitor at week 8 of treatment

- **Drug Interactions:**
  - Contraindicated HIV medications
    - All HIV protease inhibitors
    - Non-Nucleoside Reverse Transcriptase Inhibitors: efavirenz, etravirine, nevirapine
  - Rosuvastatin: do not exceed 10mg

http://www.hepatitis.uw.edu
Velpatasvir/Sofosbuvir (VEL/SOF; Epclusa®)

- FDA approved on 6/28/16
- Indications:
  - FDA approved for genotypes 1 and 4 with and without compensated cirrhosis
  - Decompensated cirrhosis (with RBV)
- Dosing: 1 tablet (VEL 100mg/SOF 400mg) daily with or without food

http://www.hepatitisc.uw.edu
Velpatasvir/Sofosbuvir

- **Adverse Effects**
  - Common: Headache, fatigue
  - Less common: rash, depression

- **Warnings/Precautions:**
  - Serious symptomatic bradycardia with amiodarone
  - Not recommended with severe renal impairment (GFR <30 ml/min/1.73m2)

- **Drug interactions**
  - Contraindicated with amiodarone
  - Acid-reducing agents***

http://www.hepatitisc.uw.edu
Ribavirin

- FDA approved in 1998
- Purine nucleoside analog, complete mechanism of action unknown
- FDA approved for GT1-6
- Dosing:
  - Weight-based dose adjustment
    - ≥75kg: 1200mg daily
    - <75kg: 1000mg daily
  - Renal dose adjustment
    - Creatinine Clearance ≤30ml/min: 200mg daily
  - Take with food
Ribavirin

- Adverse effects:
  - Hemolytic anemia (black box warning (BBW)), photosensitivity, pancreatitis, retinopathy, insomnia, fatigue, rash, pruritis

- Warnings/Precautions:
  - Teratogenicity up to 6 months following treatment (BBW)
  - Anemia
  - Hepatic Failure
  - Sensitivity

- Drug interactions:
  - Other drugs contributing anemia
  - didanosine
### Birth Control Options while on Ribavirin AND 6 months after Ribavirin

<table>
<thead>
<tr>
<th>Option 1</th>
<th>Methods to Use Alone</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Intrauterine devices (IUDs)</td>
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<tr>
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<td>Tubal sterilization</td>
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<td>Patient’s partner had a vasectomy</td>
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**OR**

<table>
<thead>
<tr>
<th>Option 2</th>
<th>Choose One Hormone Method AND One Barrier Method</th>
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<tbody>
<tr>
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<td><strong>Hormone Methods</strong> choose 1</td>
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<tr>
<td></td>
<td><strong>Barrier Methods</strong> choose 1</td>
</tr>
<tr>
<td></td>
<td>Estrogen and Progesterone</td>
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<tr>
<td></td>
<td>- Oral contraceptive pill</td>
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<tr>
<td></td>
<td>- Transdermal patch</td>
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<tr>
<td></td>
<td>- Vaginal ring</td>
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<tr>
<td></td>
<td>Progesterone-only</td>
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<tr>
<td></td>
<td>- Injection</td>
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<tr>
<td></td>
<td>- Implant</td>
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<td><strong>Barrier Methods</strong> choose 1</td>
</tr>
<tr>
<td></td>
<td>- Diaphragm with spermicide</td>
</tr>
<tr>
<td></td>
<td>- Cervical cap with spermicide</td>
</tr>
<tr>
<td></td>
<td>- Contraceptive sponge</td>
</tr>
<tr>
<td></td>
<td>- Male condom</td>
</tr>
<tr>
<td></td>
<td>- Female condom</td>
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</table>

**OR**

<table>
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<tr>
<th>Option 3</th>
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<tbody>
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<td><strong>Barrier Methods</strong> choose 1</td>
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<td>- Diaphragm with spermicide</td>
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<td>- Cervical cap with spermicide</td>
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<td><strong>Barrier Methods</strong> choose 1</td>
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<td></td>
<td>- Male condom</td>
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<tr>
<td></td>
<td>- Female condom</td>
</tr>
</tbody>
</table>

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For information only. Not to replace the advice of your health care provider.

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HCV DAA Monitoring

- 4 weeks and as indicated
  - CBC
  - Creatinine
  - Calculated GFR
  - Hepatic function panel
  - HCV RNA
- If HCV RNA is detectable at week 4, repeat in 2 weeks
- Zepatier® (EBR/GZR): hepatic function panel at 8 weeks
- 12 weeks (or end of treatment)
  - HCV RNA
- 12 weeks after treatment (SVR12)
  - HCV RNA
- HBV DNA levels for patients HBsAg + during and after HCV treatment

# Financial Support

<table>
<thead>
<tr>
<th>Medication</th>
<th>Copay Card*</th>
<th>Patient Assistance Program (for uninsured or underinsured)</th>
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</thead>
<tbody>
<tr>
<td>Sovaldi™</td>
<td>Yes ($5/month)</td>
<td>Support Path™</td>
</tr>
<tr>
<td>Olysio™</td>
<td>Yes ($5/month)</td>
<td>Janssen Prescription Assistance™</td>
</tr>
<tr>
<td>Ribavirin</td>
<td>Yes ($5/month - for brand name Moderiba™ only)</td>
<td>AbbVie Patient Assistance Foundation™</td>
</tr>
<tr>
<td>Viekira Pak™</td>
<td>Yes ($5)</td>
<td>Proceed™</td>
</tr>
<tr>
<td>Technivie™</td>
<td>Yes ($5)</td>
<td>Proceed™</td>
</tr>
<tr>
<td>Daklinza™</td>
<td>Yes ($0 - up to $5000/month)</td>
<td>BMS CONNECT™</td>
</tr>
<tr>
<td>Zepatier™</td>
<td>Yes ($5)</td>
<td>Merck Access Program™</td>
</tr>
<tr>
<td>Epclusa™</td>
<td>Yes ($5)</td>
<td>SupportPath™</td>
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*Copay Cards are only available to those without government-funded insurance*
# Grant Funding

<table>
<thead>
<tr>
<th>Grant</th>
<th>Patient Cost</th>
<th>Information</th>
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<tr>
<td>Patient Access Network Foundation (PANF)</td>
<td>$0</td>
<td><a href="https://pharmacyportal.panfoundation.org/Home.aspx">https://pharmacyportal.panfoundation.org/Home.aspx</a></td>
<td>-Max of $30,000/year &lt;br&gt;-Reside in US &lt;br&gt;-Income below 400% or 500% FPL &lt;br&gt;-Any insurance</td>
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<tr>
<td>Patient Advocate Foundation (PAF)</td>
<td>$0</td>
<td><a href="https://www.copays.org/diseases/hepatitis-c">https://www.copays.org/diseases/hepatitis-c</a></td>
<td>-Max of $25,000/year &lt;br&gt;-Reside in US &lt;br&gt;-Income below 400% FPL &lt;br&gt;-Any insurance</td>
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<tr>
<td>Chronic Disease Fund (CDF)</td>
<td>Based on poverty percentage-up to $50</td>
<td><a href="http://www.mygooddays.org/for-patients/patient-assistance/">http://www.mygooddays.org/for-patients/patient-assistance/</a></td>
<td>-Max of $30,000/year &lt;br&gt;-Reside in US &lt;br&gt;-Any insurance, must pay at least 50% of copay &lt;br&gt;-Income below 500% FPL</td>
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<tr>
<td>Healthwell Foundation</td>
<td>$5/fill</td>
<td><a href="https://www.healthwellfoundation.org/fund/hepatitis-c/">https://www.healthwellfoundation.org/fund/hepatitis-c/</a></td>
<td>-Max of $30,000/year &lt;br&gt;-Reside in US &lt;br&gt;-Any insurance &lt;br&gt;-Income below 500% FPL</td>
</tr>
</tbody>
</table>
Other Access Resources

- National Viral Hepatitis Roundtable
  - NVHR.org/hepatitis-c-treatment-access
- Hepatitis C New Drug Research
- American Liver Foundation
  - http://hepc.liverfoundation.org/resources/what-if-i-need-financial-assistance-to-pay-for-treatment/
- Life Beyond Hepatitis C
Outline

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HCV Medication Interactions

HEP Drug Interactions

HEP Drug Interaction Checker
Access our comprehensive, user-friendly, free drug interaction charts. Providing clinically useful, reliable, up-to-date, evidence-based information

Start Now →
HCV Medication Interactions

- Acid-reducing agents
- Anticonvulsants
- Amiodarone, digoxin
- Azole antifungals
- Statins

*AASLD/IDSA Guidelines*
Outline

- HCV epidemiology and biology
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## HCV GT 1a, Treatment Naïve

<table>
<thead>
<tr>
<th>Fibrosis</th>
<th>Recommended Treatment</th>
<th>Treatment Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>F0-F3 (Non-cirrhotic)</td>
<td>DCV (Daklinza™) + SOF (Sovaldi™)</td>
<td>12 weeks</td>
</tr>
<tr>
<td></td>
<td>EBR/GZP (Zepatier™)</td>
<td>12 weeks*</td>
</tr>
<tr>
<td></td>
<td>LDV/SOF (Harvoni™)</td>
<td>12 weeks**</td>
</tr>
<tr>
<td></td>
<td>PrOD (Viekira Pak/XR™) + RBV</td>
<td>12 weeks</td>
</tr>
<tr>
<td></td>
<td>SOF (Sovaldi™) + SMV (Olysio™)</td>
<td>12 weeks</td>
</tr>
<tr>
<td></td>
<td>SOF/VEL (Epclusa™)</td>
<td>12 weeks</td>
</tr>
</tbody>
</table>

* - If no NS5A resistance-associated variants detected. ** - Consider 8 weeks in select patients.
## HCV GT 1a, Treatment Naïve

<table>
<thead>
<tr>
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* - If no NS5A resistance-associated variants detected. ** - Consider 8 weeks in select patients.

## HCV GT 1a, P/R Treatment Experienced

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## HCV GT 1b, Treatment Naïve

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<td><em>Alternative:</em> SOF (Sovaldi™) + DCV (Daklinza™)</td>
<td>16-24 weeks</td>
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### HCV GT 2: P/R Treatment Experienced

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# HCV GT 3: Treatment Naïve

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<td>F4 (Cirrhotic)</td>
<td>DCV (Daklinza™) + SOF (Sovaldi™) +/- RBV</td>
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HCV GT 3: P/R Treatment Experienced

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## HCV GT 4: Treatment Naïve

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# HCV GT 4: Treatment Experienced

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<tr>
<td>F0-F4</td>
<td>EBV/GZR (Zepatier™) - Previous relapse on Peg-IFN/RBV</td>
<td>12 weeks</td>
</tr>
<tr>
<td></td>
<td>EBV/GZR (Zepatier™) + RBV - Prior on-treatment virologic failure</td>
<td>16 weeks</td>
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<td>LDV/SOF (Harvoni™)</td>
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HCV GT 5, 6: Treatment Naïve or Experienced

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HCV Pipeline

- Focus on difficult-to-treat populations
  - Genotype 3 cirrhosis
  - Decompensated cirrhosis
  - End stage renal disease
- Shorter duration of treatment
- Pan-genotypic
Outline

- HCV epidemiology and biology
- HCV Treatment Considerations
- Currently Available Direct Acting Antivirals (DAA)
- DAA medication interactions
- Current HCV treatment regimens
- Special Populations
HIV/HCV Coinfection

- Same regimens as used for HCV monoinfection
- Efficacy similar between HCV monoinfection and HIV/HCV coinfection populations
- HIV antiretroviral therapy (ART) should not be interrupted
- Special attention to drug-drug interactions
  - Avoid “double dosing” RTV when using RTV-boosted DAA therapy (i.e. paritaprevir)
  - Adjust DCV dose based on concomitant ART
  - Monitor impact of DAA and ART on TDF

Slide adapted from Cody Chastain, MD.
Renal Impairment and HCV

- **Mild to moderate impairment:**
  - CrCl 30-80ml/min
  - No dose adjustment necessary to currently approved Direct Acting Antivirals (DAA)

- **Severe impairment:**
  - CrCl <30ml/min
  - Considerations for sofosbuvir-containing regimens and ribavirin

- **Treatment options in clinical practice may differ between patients with severe renal impairment (CrCl 10-30 ml/min) and those with CKD stage 5 / end stage renal disease (although not differentiated in HCV Guidelines).**
Retreatment of DAA Failures

- Strongly consider referral to expert HCV treater
- Treatment approach depends on:
  - Prior DAA regimen
  - Duration of prior DAA regimen
  - Stage of liver disease
  - Prior adherence
  - Drug-drug interactions
  - Baseline and/or acquired resistance-associated variants (RAVs)
  - Anticipated DAA approvals

Slide adapted from Cody Chastain, MD.
Decompensated Cirrhosis

- Refer to experienced hepatology and HCV provider, ideally in at a liver transplant center
- Avoid HCV therapies that are contraindicated in decompensated cirrhosis:
  - IFN
  - Telaprevir
  - Boceprevir
  - Simeprevir
  - Paritaprevir/ritonavir/Ombitasvir + Dasabuvir
  - Elbasvir/Grazoprevir
- Treatment may impact transplant eligibility and status
Education and Counseling

- Transmission
- Natural history
- Alcohol and substance use abstinence
- HAV and HBV vaccination

Available resources
- Centers for Disease Control
- American Liver Foundation
- Veterans Affairs
HCV Prevention and Screening

- No available vaccine
- Use universal precautions, avoid high-risk sexual behavior, and avoid IVDU
- Poor outcomes related to chronic HCV infection may be reduced by abstaining from alcohol and hepatotoxic medications
Summary

- HCV treatment has transformed over the past several years.
- High efficacy therapies with limited side effects are available for all genotypes.
- Select HCV treatment is based on primary (genotype, stage, treatment experience) and secondary factors.
- Strongly consider referral of special patient populations to an expert.
- Though costly, the price of HCV treatment should not limit prescribing of these medications.
Questions?

Autumn Bagwell, PharmD, BCPS, AAHIVP
Autumn.D.Bagwell@vanderbilt.edu