Treatment and Management of Hepatitis C Genotype 1: A Primer for Pharmacists

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Disclosures

I, Katelyn Simmons, do not have any actual or potential conflicts of interest in relation to this presentation
Objectives

By the end of this presentation, the participant will be able to:

- Recognize the prevalence and pathophysiology of hepatitis C virus (HCV)
- Apply knowledge of the direct acting antivirals’ most common drug interactions, contraindications, side effects, and how to manage them
- Illustrate current barriers to care and controversies surrounding HCV treatment
Outline

- Epidemiology
- Disease Overview
- Pathophysiology
- Direct Acting Antiviral Agents
- Guidelines
- Special Populations
- Cost
- Current Controversy
Case Introduction

- 65 year old white man
- Presents to primary care physician (PCP) for annual check-up with complaints of more tiredness than usual over the past few weeks
Case Introduction

PMH
- Hypothyroidism
- Hyperlipidemia
- GERD
- Depression
- Type 2 diabetes mellitus (T2DM)
- Chronic kidney disease, secondary to T2DM

Medications
- Levothyroxine 125mcg daily
- Rosuvastatin 10mg daily
- Omeprazole 20mg daily
- Metformin 1000mg BID
- Lisinopril 2.5mg daily

FH
- Mother: alive, well
- Father: Died (MI) at age 60

SH
- Retired engineer
- Alcohol: >8 drinks/week socially
- Tobacco: Denies
HCV - Epidemiology

- ~170 million people worldwide
- Most common reason for chronic liver disease and liver transplant in the U.S.
- Leading cause of hepatocellular carcinoma (HCC)
  - Now the #2 cause of cancer death worldwide
- Increases all cause mortality

Yearly New Infections of HCV

HCV - Epidemiology

- Prevalence higher among blacks (5.6%) than in Hispanics or whites (2.7%)
- The "baby-boomers" have a significantly higher prevalence, especially those born between 1950 and 1965 (3.61%)
- GT 1 ~70% of all cases in U.S.

HCV - Pathophysiology

- Infection of the liver caused by HCV
- Spread primarily through infected blood and needles
- Incubation period: 3-20 weeks from infection
- Mechanism of liver injury is not well understood
  - Direct effect of the virus and immune-mediated injury
  - Extrahepatic manifestations due to immune complex-mediated tissue injury
- Infection does not provide immunity

HCV - Risk Factors

- Screening
  - Born between 1945 and 1965
  - Based on risk factors for others
  - Evidence of liver disease

<table>
<thead>
<tr>
<th>Risk Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Injection-drug use</td>
</tr>
<tr>
<td>Birth cohort from 1945-1965</td>
</tr>
<tr>
<td>HIV coinfection</td>
</tr>
<tr>
<td>Unscreened blood product transfusion</td>
</tr>
<tr>
<td>Healthcare occupations</td>
</tr>
<tr>
<td>Sex with infected partners</td>
</tr>
<tr>
<td>Hemodialysis</td>
</tr>
<tr>
<td>Poor socioeconomic status</td>
</tr>
<tr>
<td>Incarcerated</td>
</tr>
</tbody>
</table>

## Testing and Diagnosis

<table>
<thead>
<tr>
<th>Assay for HCV Antibody</th>
<th>Quantitative HCV RNA</th>
</tr>
</thead>
<tbody>
<tr>
<td>If reactive or intermediate, test for HCV RNA</td>
<td>If detected, infection confirmed</td>
</tr>
<tr>
<td>Simultaneously test HCV RNA if high suspicion for infection or false negative</td>
<td>If not detected, false antibody test or HCV previously cleared</td>
</tr>
</tbody>
</table>

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**Assay for HCV Antibody**

- If reactive or intermediate, test for HCV RNA
- Simultaneously test HCV RNA if high suspicion for infection or false negative

**Quantitative HCV RNA**

- If detected, infection confirmed
- If not detected, false antibody test or HCV previously cleared

---


HCV - Clinical Presentation

- Majority (80%) are asymptomatic
- Acute hepatitis
  - Symptoms: Fatigue, loss of appetite, abdominal pain, nausea, dark urine, and jaundice
- Chronic hepatitis
- Cirrhosis
- Complications: HCC or extrahepatic manifestations

HCV - Cirrhosis

- A condition in which the liver slowly deteriorates and malfunctions due to chronic injury
  - Scar tissue replaces healthy liver tissue, partially blocking the flow of blood through the liver
- Causes: Heavy alcohol consumption, chronic HCV, obesity
  - Many have >1 cause
- 12th leading cause of death by disease

Back to the Case

- Which risk factors does our patient have?
- Which symptoms?
- Is this patient a candidate for HCV screening?
# Case - Objective

## Pertinent Labs

<table>
<thead>
<tr>
<th>Test</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TSH</td>
<td>1 mIU/L</td>
</tr>
<tr>
<td>HbA1C</td>
<td>6.8%</td>
</tr>
<tr>
<td>TC</td>
<td>160 mg/dL</td>
</tr>
<tr>
<td>LDL</td>
<td>89 mg/dL</td>
</tr>
<tr>
<td>HDL</td>
<td>43 mg/dL</td>
</tr>
<tr>
<td>TG</td>
<td>107 mg/dL</td>
</tr>
<tr>
<td>AST</td>
<td>115 IU/L</td>
</tr>
<tr>
<td>ALT</td>
<td>190 IU/L</td>
</tr>
<tr>
<td>K+</td>
<td>4.5 mEq/L</td>
</tr>
<tr>
<td>sCr</td>
<td>1.4 mg/dL</td>
</tr>
<tr>
<td>CrCl</td>
<td>64.4 mL/min</td>
</tr>
<tr>
<td>TC</td>
<td>160 mg/dL</td>
</tr>
<tr>
<td>LDL</td>
<td>89 mg/dL</td>
</tr>
<tr>
<td>HDL</td>
<td>43 mg/dL</td>
</tr>
<tr>
<td>TG</td>
<td>107 mg/dL</td>
</tr>
</tbody>
</table>

## Vitals

<table>
<thead>
<tr>
<th>Test</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood Pressure</td>
<td>134/72 mmHg</td>
</tr>
<tr>
<td>Heart Rate</td>
<td>72 bpm</td>
</tr>
<tr>
<td>Height</td>
<td>72 in</td>
</tr>
<tr>
<td>Weight</td>
<td>220 lb</td>
</tr>
<tr>
<td>Height</td>
<td>72 in</td>
</tr>
<tr>
<td>Weight</td>
<td>220 lb</td>
</tr>
</tbody>
</table>
Case - Objective

- Ultrasound: normal liver

<table>
<thead>
<tr>
<th>HCV Labs</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total Protein</strong></td>
<td>6.7 g/dL</td>
<td>Anti-HCV POS</td>
<td>115 IU/L</td>
</tr>
<tr>
<td><strong>Albumin</strong></td>
<td>4.3 g/dL</td>
<td>HCV RNA</td>
<td>2,500,000 IU/L</td>
</tr>
<tr>
<td><strong>Bilirubin</strong></td>
<td>0.9 mg/dL</td>
<td>GT</td>
<td>1a</td>
</tr>
<tr>
<td><strong>INR</strong></td>
<td>1.0</td>
<td>CBC</td>
<td>WNL</td>
</tr>
</tbody>
</table>
Do you decide to treat?

To be continued....
Assessment Question #1

Approximately what percentage of patients living with HCV were born from 1945 to 1965?

A. 50%
B. 66%
C. 75%
D. 90%
Assessment Question #2

What is currently the most common risk factor for HCV acquisition?

A. Sexually transmitted diseases
B. Injection drug use
C. Blood transfusion(s)
D. Poor socioeconomic status
HCV GT1- Treatment
Evolution of Hepatitis C Treatment

1997 - 2013
- Interferon (IFN) based therapies
- Protease inhibitors in 2011
- Used +/- ribavirin (RBV)

2014
- 1st daily DAA, Harvoni®
- Viekira Pak™

2015-16
- Daklinza™
- Epclusa®
- Zepatier™

HCV - Goals of Treatment

- **Goal:** Achieve sustained virologic response (SVR)
  - HCV RNA level virtually undetectable 12+ weeks after completing antiviral treatment
- **Successful antiviral treatment of chronic HCV infection decreases the risk of disease progression and death**

Ng V, Saab S. Effects of a sustained virologic response on outcomes of patients with chronic hepatitis C. Clin Gastroenterol Hepatol 2011; 9:923.
Treatment Recommendations
Patient Considerations

Candidates for antiviral treatment:
- Any chronic HCV patient with a life expectancy > 12 months

Urgency may depend on several factors:
- Risk of developing decompensated cirrhosis
- Risk of dying from liver or liver-related disease
- Prolonging graft survival in liver transplant patients
Patient Considerations

▶ Ongoing substance use: not an automatic exclusion
  ▶ Alcohol, illicit drugs, marijuana, opioid replacement program

▶ May need to address prior to treatment:
  ▶ Risk of non-adherence
  ▶ Risk of re-infection
  ▶ Greater clinical urgency
Direct Acting Antivirals
Direct Acting Antivirals

- Sofosbuvir (Sovaldi®)
- Simeprevir (Olysio®)
- Ledipasvir/sofosbuvir (Harvoni®)
- Paritaprevir/ritonavir/ombitasvir plus dasabuvir (Viekira Pak™)
- Daclatasvir (Daklinza™) plus sofosbuvir (Sovaldi®)
- Elbasvir/grazoprevir (Zepatier™)
- Sofosbuvir/velpatasvir (Epclusa®)
Sovaldi® (sofosbuvir)
Sovaldi®

- Approved for use in combinations December, 2013
- Component of 2 DAAs and used with 2 other DAAs

<table>
<thead>
<tr>
<th>MOA</th>
<th>Non-structural viral protein 5B (NS5B) polymerase inhibitor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dosing</td>
<td>400mg daily</td>
</tr>
<tr>
<td>Use</td>
<td>Treatment naïve or experienced, +/- cirrhosis</td>
</tr>
<tr>
<td>Adjustments</td>
<td>None</td>
</tr>
<tr>
<td>FDA approval</td>
<td>GT 1 - 4</td>
</tr>
<tr>
<td>Adverse Effects</td>
<td>Fatigue and headache</td>
</tr>
</tbody>
</table>

AASLD/IDSA. Recommendations for testing, management, and treating hepatitis C. Sovaldi (sofosbuvir) [prescribing information]. Foster City, CA; Gilead Sciences; August 2015.
Major Drug Interactions:

- **Anticonvulsants**: carbamazepine, oxycarbazepine, phenobarbital, phenytoin
- **Antimycobacterials**: rifampin
- **Herbal Supplements**: St. John's wort
- **HIV Protease Inhibitors**: tipranavir-ritonavir
Olysio® (simeprevir)
Olysio®

- Approved for use with sofosbuvir in November, 2014
- Issues with resistance similar to other protease inhibitors

<table>
<thead>
<tr>
<th>MOA</th>
<th>NS3/4A protease inhibitor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dosing</td>
<td>150mg daily with food</td>
</tr>
<tr>
<td>Use</td>
<td>Treatment naïve or experienced, +/- cirrhosis</td>
</tr>
<tr>
<td>Adjustments</td>
<td>None</td>
</tr>
<tr>
<td>FDA approval</td>
<td>GT 1</td>
</tr>
<tr>
<td>Adverse Effects</td>
<td>Rash, pruritis, nausea</td>
</tr>
</tbody>
</table>

Harvoni® (Ledipasvir/sofosbuvir)
Harvoni®

- Approved October, 2014

- Indications:
  - HCV GT 1, 4, 5, 6
  - +/- HIV
  - +/- compensated cirrhosis

- MOA: interferes with viral replication
  - Ledipasvir: NS5A inhibitor
  - Sofosbuvir: NS5B polymerase inhibitor
Harvoni®

- **Dose/Administration:**
  - A fixed-dose combination tablet (90 mg/400 mg)
  - One tablet daily, with or without food

- **Adverse effects:**
  - Fatigue (10-18%), headache (11-29%), nausea (6-9%), diarrhea (3-7%), insomnia (3-6%)


Readler, LA. Once-a-Day Harvoni (Ledipasvir plus Sofosbuvir), a New Oral Combination for the Treatment of Patients with Genotype 1 Chronic Hepatitis C Infection. Sixth Annual Payers’ Guide - Drug Updates. March 2015; volume 8.

Viekira Pak™
(Paritaprevir/ritonavir/ombitasvir + dasabuvir)
Viekira Pak™

- Approved on December 19, 2014
- Indication: HCV GT 1
  - With or without cirrhosis
  - Used with weight-based RBV
    - Except in GT 1b without cirrhosis

Viekira Pak (ombitasvir, paritaprevir, ritonavir, dasabuvir) [prescribing information]. North Chicago, IL: AbbVie Inc; June 2016.
Guidance from the American Association for the Study of Liver Diseases (AASLD) and the Infectious Disease Society of America (IDSA) Recommendations for Testing, Managing, and Treating hepatitis C. Available online at http://www.hcvguidelines.org/full-report-view [Accessed December 10, 2016]
Ritonavir 100 mg - CYP3A inhibitor to boost paritaprevir levels

Paritaprevir - a NS3/4A protease inhibitor
Dasabuvir - nonnucleoside NS5B polymerase inhibitor

Ombitasvir - NS5A inhibitor

Viekira Pak™

Viekira Pak (ombitasvir, paritaprevir, ritonavir, dasabuvir) [prescribing information]. North Chicago, IL: AbbVie Inc; June 2016.
Guidance from the American Association for the Study of Liver Diseases (AASLD) and the Infectious Disease Society of America (IDSA) Recommendations for Testing, Managing, and Treating hepatitis C. Available online at http://www.hcvguidelines.org/full-report-view [Accessed December 19, 2016]
Viekira Pak™

Common Adverse Reactions
Asthenia, fatigue, pruritus, nausea, and insomnia

Laboratory Monitoring Prior to Treatment
Transaminase and total and direct bilirubin levels
Hemoglobin levels if used with RBV

Renal/Hepatic Impairment
No dose adjustments in renal impairment
Has not been studied in end-stage renal disease or dialysis
No dose adjustment in mild liver impairment

Viekira Pak (ombitasvir, paritaprevir, ritonavir, dasabuvir) [prescribing information]. North Chicago, IL: AbbVie Inc; June 2016.
Contraindications

- Severe hepatic impairment

Contraindications with certain medications

- Drugs highly dependent on CYP3A for clearance
- Moderate and strong inducers of CYP3A
- Strong inducers and inhibitors of CYP2C8

Contraindications to RBV may also apply

- Pregnancy
- Autoimmune hepatitis
- Hemoglobinopathies
- CrCl <50 mL/min
- Coadministration with didanosine
- Hypersensitivity

Viekira Pak™

Viekira Pak (ombitasvir, paritaprevir, ritonavir, dasabuvir) [prescribing information]. North Chicago, IL: AbbVie Inc; June 2016.
Daklinza\textsuperscript{TM} (Daclatasvir) + Sovaldi\textsuperscript{®} (sofosbuvir)
Daklinza™ + Sovaldi®

- **Daclatasvir**
  - FDA approved on July 24, 2015
  - Indicated for chronic HCV GT 1 or 3 infection
    - With sofosbuvir
    - With or without RBV
  - Available in 30mg and 60mg tablets
    - Dose is 60mg once daily with or without food
    - When used with daclatasvir, the dosing of sofosbuvir is 400mg once daily

Daklinza™ + Sovaldi®

Treatment for HCV GT 1

<table>
<thead>
<tr>
<th>Indication</th>
<th>Treatment Regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Without cirrhosis</td>
<td>Daclatasvir plus sofosbuvir x 12 weeks</td>
</tr>
<tr>
<td>Compensated (Child-Pugh A) cirrhosis*</td>
<td>Daclatasvir plus sofosbuvir x 12 weeks</td>
</tr>
<tr>
<td>Decompensated (Child-Pugh B or C) cirrhosis*</td>
<td>Daclatasvir plus sofosbuvir + RBV x 12 weeks</td>
</tr>
<tr>
<td>Post-transplant</td>
<td>Daclatasvir plus sofosbuvir + RBV x 12 weeks</td>
</tr>
</tbody>
</table>

*If patients have GT 1a and cirrhosis, consider screening for baseline NS5A resistance-associated polymorphisms.

Daklinza™ + Sovaldi®

- Daclatasvir is an NS5A inhibitor
- Believed to inhibit viral RNA replication and virion assembly

Daklinza (daclatasvir) [prescribing information]. Princeton, NJ: Bristol-Myers Squibb Co; February 2016.
Daklinza™

Adverse effects
• Fatigue
• Headache
• Nausea
• Diarrhea

Contraindications
• Use with strong inducers of CYP3A4
  • Phenytoin
  • Carbamazepine
  • Rifampin
  • St. John’s Wort

Dose Adjustments
• None for renal impairment
• None for hepatic impairment

Zepatier™ (Elbasvir/grazoprevir)
Zepatier™

- Indicated for chronic HCV GT 1 and 4 in adults
- FDA approved on January 28, 2016
- Dosing
  - 100 mg/50 mg tablet once daily for 12 or 16 weeks
  - Take with or without food
  - Some regimens require addition of RBV

Zepatier™

- Elbasvir - NS5A inhibitor
- Grazoprevir - NS3/4A protease inhibitor
- Baseline high fold change NS5A resistance-associated variants (RAVs) must be undetectable
  - 10-15% of HCV GT 1 patients without prior exposure to NS5A inhibitors have detectable HCV NS5A RAVs
    - RAV causes a >5 fold reduction in activity of NS5A inhibitors
### Zepatier™

#### Common Adverse Reactions
- Fatigue, headache, and nausea

#### Contraindications
- Moderate or severe hepatic impairment
- Use with OATP1B1/3 inhibitors and strong CYP3A4 inducers

#### Hepatic/Renal Impairment
- No dose adjustment in mild hepatic impairment (Child-Pugh Class A)
- Can be used in severe renal impairment
  - CKD stage 4 or 5
Epclusa® (sofosbuvir/velpatasvir)
Epclusa®

- Approved on June 28, 2016
- MOA: sofosbuvir, NS5B polymerase inhibitor, and velapatasvir, NS5A replication complex inhibitor
- Indications: HCV GT 1-6
  - Without cirrhosis and with compensated cirrhosis: 12 weeks
  - With decompensated cirrhosis: With RBV x 12 weeks
- Dosing
  - Once daily, fixed-dose combination tablet of sofosbuvir-velpatasvir 400 mg/100 mg

Epclusa (sofosbuvir and velpatasvir) [prescribing information]. Foster City, CA: Gilead Sciences Inc; June 2016
Epclusa® - Indications

- MOA: sofosbuvir, NS5B polymerase inhibitor and velpatasvir, NS5A replication complex inhibitor
Epclusa®

Adverse Effects
- Headache, fatigue; less commonly nausea, irritability

Hepatic/Renal Impairment
- No dose adjustment with mild-moderate renal impairment
- Insufficient data in patients with severe renal impairment
- No dose adjustment with hepatic impairment
Clinical Application
Drug Interactions

- **All DAAs:** HIV antiretrovirals, anticonvulsants (carbamazepine, phenytoin, phenobarbital, etc), certain herbals (St. John’s Wort)
- **All but Sovaldi®:** certain statins
- **Amiodarone:** avoid with any agent containing sofosbuvir (Harvoni®, Sovaldi® itself) and with Daklinza™
- **Antacids:** specific dosing instructions with Harvoni® and Epclusa®
- **Contraindicated with strong CYP3A4 inducers:**
  - Daklinza™, Zepatier®, Viekira Pak™
- See handout for more detailed information
Guideline Recommendations for Treatment
HCV - Guidelines

- American Association for the Study of Liver Diseases (AASLD) and Infectious Diseases Society of America (IDSA) Recommendations for Testing, Managing, and Treating Hepatitis C
- Constantly evolving and updating
- www.hcvguidelines.org
Initial Treatment of HCV GT 1

- Six highly potent direct-acting antiviral (DAA) oral combination regimens
  - Treatment based upon:
    - HCV subtype
    - Presence of cirrhosis
    - Presence or absence of NS5A resistance-associated variants (RAV)
      - Strongest predictor of treatment success with certain regimens

Decompensated cirrhosis?

NO

Subtype 1a

No cirrhosis

Harvoni x 12 wks
Epclusa x 12 wks
Zepatier x 12 wks
Viekira Pak* x 12 wks
Olysio + Sovaldi x 12 wks
Daklinza + Sovaldi x 12 wks

Cirrhosis

Harvoni x 12 wks
Epclusa x 12 wks
Zepatier x 12 wks
Viekira Pak x 12 wks
Olysio + Sovaldi x 12 wks
Daklinza + Sovaldi x 12 wks

Subtype 1b

No cirrhosis

Harvoni x 12 wks
Epclusa x 12 wks
Zepatier x 12 wks
Viekira Pak x 12 wks
Olysio + Sovaldi x 12 wks
Daklinza + Sovaldi x 12 wks

Cirrhosis

Harvoni x 12 wks
Epclusa x 12 wks
Zepatier x 12 wks
Viekira Pak x 12 wks
Olysio + Sovaldi x 12 wks
Daklinza + Sovaldi x 12 wks

• with RBV

Treatment of HCV GT 1- Summary

- Almost all patient with HCV may benefit from therapy
  - Sole exception are patients with an expected lifespan < 1 year
Treatment of HCV GT 1- Summary

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  - Sole exception are patients with an expected lifespan < 1 year
- New DAA, IFN-free regimens are now the standard of care
Treatment of HCV GT 1- Summary

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- For initial therapy of treatment-naive patients without cirrhosis, six 12-week regimens with similar efficacy are recommended in the AASLD/IDSA guidance
Treatment of HCV GT 1- Summary

- Almost all patients with HCV may benefit from therapy
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- New DAA, IFN-free regimens are now the standard of care
- For initial therapy of treatment-naive patients without cirrhosis, six 12-week regimens with similar efficacy are recommended in the AASLD/IDSA guidance
- For initial therapy of treatment-naive patients with compensated cirrhosis, three 12-week regimens with similar efficacy are recommended
Treatment of HCV GT 1 - Summary

- Almost all patients with HCV may benefit from therapy
  - Sole exception are patients with an expected lifespan < 1 year
- New DAA, IFN-free regimens are now the standard of care
- For initial therapy of treatment-naive patients without cirrhosis, six 12-week regimens with similar efficacy are recommended in the AASLD/IDSA guidance
- For initial therapy of treatment-naive patients with compensated cirrhosis, three 12-week regimens with similar efficacy are recommended
- High cost is the major barrier to treatment with all new DAAs
Case - What would you pick for initial treatment?
Things to Consider…..

- Treatment naïve
- No cirrhosis
- No significant renal impairment
- No HIV co-infection
Options:

- Harvoni® x 12 wks
- Epclusa® x 12 wks
- Zepatier® x 12 wks
- Viekira Pak™* x 12 wks
- Olysio® + Sovaldi® x 12 wks
- Daklinza™ + Sovaldi® x 12 wks
Game-Changers

- What would you select if:
  - The patient was found to have Child-Pugh Class C cirrhosis?
  - He had HIV?
  - His serum creatinine bumped to 3.4 mg/dL?
## Specific Treatment Considerations

<table>
<thead>
<tr>
<th>Special Population</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV</td>
<td>Assess drug-drug interactions</td>
</tr>
<tr>
<td>Not suppressed on HIV antiretroviral therapy</td>
<td>Do NOT use Viekira Pak™</td>
</tr>
<tr>
<td>Severe renal impairment or end-stage requiring dialysis</td>
<td>Do NOT use sofosbuvir-containing regimens</td>
</tr>
<tr>
<td>Moderate-severe hepatic impairment</td>
<td>Do NOT use Zepatier® or Viekira Pak™</td>
</tr>
<tr>
<td>Cirrhosis</td>
<td>Extended durations of treatment and/or addition of RBV</td>
</tr>
<tr>
<td>Post-transplant</td>
<td>Harvoni® + RBV x 12 weeks or Harvoni® x 24 weeks</td>
</tr>
</tbody>
</table>
HCV with Renal Impairment

- Dialysis is a major risk factor for HCV
- Renal function must be assessed before initiating any HCV treatment
- Mild - moderate renal impairment: Standard doses recommended
- Severe renal impairment: Adjustments needed
### Monitoring

<table>
<thead>
<tr>
<th>Prior to initiation of treatment</th>
<th>Within 12 weeks prior to starting therapy</th>
<th>At 4 weeks of treatment</th>
<th>12 weeks following completion of therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Quantitative HCV viral load</td>
<td>• Complete blood count (CBC)</td>
<td>• Quantitative HCV viral load</td>
<td></td>
</tr>
<tr>
<td>• Assessment of fibrosis severity</td>
<td>• International normalized ratio (INR)</td>
<td>• CBC</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Hepatic function panel (HFP)</td>
<td>• Serum creatinine</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Glomerular filtration rate (GFR)</td>
<td>• GFR</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• HFP</td>
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</tr>
</tbody>
</table>

Case - What would you include as key counseling points prior to his first fill?
Cost Effectiveness
Cost-Effectiveness

- The newest DAA medications are among of the most expensive oral medications in history

- The wholesale acquisition costs (WAC) are substantially higher than estimated production costs for the medications
  - WAC for 12 weeks of sofosbuvir: $84,000
  - Production cost: $68-136

- New DAAs have been highly effective in treating chronic HCV, but the high cost of these medications has been a significant barrier to widespread treatment access
### Estimated Cost for Treatment of HCV GT 1

<table>
<thead>
<tr>
<th>Treatment Regimen</th>
<th>Cost based on WAC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daklinza™ + Sovaldi® x 12 weeks</td>
<td>$147,000</td>
</tr>
<tr>
<td>Zepatier® x 12 weeks</td>
<td>$54,600</td>
</tr>
<tr>
<td>Harvoni® x 12 weeks</td>
<td>$94,000</td>
</tr>
<tr>
<td>Viekira Pak™ x 12 weeks</td>
<td>$84,000</td>
</tr>
<tr>
<td>Olysio® + Sovaldi® x 12 weeks</td>
<td>$150,000</td>
</tr>
<tr>
<td>Epclusa® x 12 weeks</td>
<td>$74,760</td>
</tr>
</tbody>
</table>
Cost-Effectiveness

- A cost-effective strategy may be treatment of all patients with HCV
  - Not plausible due to financial constraints
- The wholesale acquisition cost (WAC) for each the new DAAs ranges from $750 - $1125/day
- Universal treatment is neither feasible nor affordable at the current prices

Current Challenges and Controversies

- Selective approvals
  - In multiple states, Medicaid denied ~50% of all claims
  - Many insurance and Medicaid programs were/are only approving DAAs for HCV treatment for patients with advanced fibrosis
- The approval process for DAAs for patients with HCV can be confusing and time-consuming
- Generalist vs. specialist prescribing
  - Insufficient specialists to handle the HCV population

Return to Case- Medications

- Which of our patient’s medications may pose a problem when selecting initial HCV therapy?
  - Levothyroxine 0.125mcg daily
  - Rosuvastatin 10mg daily
  - Omeprazole 20mg daily
  - Metformin 1000mg BID
  - Lisinopril 2.5mg daily

- Are there other medications that this patient could be taking, based on his disease states, that would interact with his options for HCV treatment?
HCV Patient Resources

- HELP-4-HEP
  - Staffed by trained counselors
- The HCV Advocate
  - Fact sheets and booklets
- Hep C Association
  - News and information
- Harbor Path - harborpath.org
  - Single site for all HIV and HCV assistance applications
- Patient Advocate Foundation
  - www.copways.org/diseases/hepatitis-c
Questions?

Thank you!

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