EXAMINING THE 3 Cs OF HEPATITIS C: CARE, CURE, CO$T

Update presented by
Lisa Townshend-Bulson, MSN, FNP-C
Followed by
Round Table Discussion:
ANTHC Liver Disease & Hepatitis Program Staff and Audience
Question #1

Is the price of new hepatitis C drugs which result in reduction of cirrhosis and decrease the risk of liver cancer, liver failure, and liver related death ... ?

A. Too low
B. Too high
C. Just right
Question #2

For which patient would you recommend hepatitis C treatment?

A. Person with mild liver fibrosis
B. Person with moderate liver fibrosis
C. Person with advanced liver fibrosis (bridging fibrosis or cirrhosis)
D. All of the above
Question #3

Would you give hepatitis C treatment to a past substance abuser?

A. Yes
B. No
Question #4

Would you give hepatitis C treatment to a current substance abuser?
A. Yes
B. No
Disclosures

• This talk will include information about investigational drugs that have not yet been approved by the FDA and one off-label practice used in the treatment of hepatitis C.

• No commercial or financial interests to disclose
Objectives

- Understand treatment medications by genotype and appropriate prescribing
- Recognize hepatitis C treatments result in cure of hepatitis C in ≥ 90% of patients now and soon ≥ 95%
- Recognize that cure of hepatitis C leads to significant decrease in liver cancer, liver failure and liver-related death
- Identify issues related to hepatitis C treatment
Glossary of Liver Disease Terms Used

- ESLD – End stage liver disease
- HCC - Hepatocellular carcinoma
- LT – Liver transplant
- NASH – Non-alcoholic steatohepatitis
- Peg - Peginterferon alfa
- Rib - Ribavirin
- Sof - Sofosbuvir
- SVR - Sustained virologic response
- TN - Treatment-naïve (never treated before)
- TE - Treatment-experienced (previously treated and either failed treatment or relapsed after)
WHAT DRUGS ARE CURRENTLY FDA APPROVED?
Sofosbuvir: Current FDA Approved Indications

<table>
<thead>
<tr>
<th>HCV and HCV/HIV Co-Infection</th>
<th>Treatment</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genotypes 1, 4 Interferon Ineligible Alternative</td>
<td>Sofosbuvir + Peginterferon (Peg) + Ribavirin (Rib)</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Genotype 2</td>
<td>Sofosbuvir + Rib</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Genotype 3</td>
<td>Sofosbuvir + Rib</td>
<td>24 weeks</td>
</tr>
</tbody>
</table>
Simeprevir:

FDA Approved Indication is with Peg/Rib for Genotype 1 only with compensated liver disease

<table>
<thead>
<tr>
<th>Patient Population</th>
<th>Simeprevir, Peg and Rib</th>
<th>+ Treatment with Peg and Rib</th>
<th>Total Treatment Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment naïve and prior relapser patients</td>
<td>First 12 weeks</td>
<td>Additional 12 weeks</td>
<td>24 weeks</td>
</tr>
<tr>
<td>Prior partial or null responder patients</td>
<td>First 12 weeks</td>
<td>Additional 36 weeks</td>
<td>48 weeks</td>
</tr>
</tbody>
</table>
## SVR Rates of FDA-Approved Treatments

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Overall SVR</th>
<th>SVR in Advanced Fibrosis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sofosbuvir-based</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Geno 1</td>
<td>89%</td>
<td>80%</td>
</tr>
<tr>
<td>Geno 2</td>
<td>93%</td>
<td>83-100% TN &amp; TE</td>
</tr>
<tr>
<td>Geno 3</td>
<td>84%</td>
<td>92% TN/60% TE</td>
</tr>
<tr>
<td>Geno 4</td>
<td>96%</td>
<td>--</td>
</tr>
<tr>
<td><strong>Simeprevir (Geno 1 only) with Peg/Rib</strong></td>
<td>77-80%</td>
<td>68-73%</td>
</tr>
</tbody>
</table>
Sofosbuvir-Based Treatment for HCV and HIV Coinfection

<table>
<thead>
<tr>
<th>Treatment (All Interferon-free)</th>
<th>Overall SVR*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Geno 1 Sof + Rib x 24 wks</td>
<td>76%, 85%</td>
</tr>
<tr>
<td>Geno 2 Sof + Rib x 12 wks</td>
<td>88%, 88%</td>
</tr>
<tr>
<td>Geno 3 Sof + Rib x 24 wks</td>
<td>92%, 89%</td>
</tr>
</tbody>
</table>

Photon 1, Photon 2 studies
Off-Label Treatments

Currently seen in practice
Simeprevir-Sofosbuvir for Genotype 1 Interferon-Ineligible

- Not currently FDA approved but is included in AASLD/IDSA Guidelines
- Sofosbuvir plus simeprevir with or without ribavirin for 12 weeks
- Based on Phase 2 Cosmos Trial (n=167)
  - SVR was 96% with ribavirin and 93% without ribavirin
Alternative Treatment for Genotype 3
AASLD/IDSA Guidelines

- Sofosbuvir plus peginterferon and ribavirin x 12 weeks
- Overall SVR (Phase 2 studies) 97%
- SVR in advanced fibrosis 83%
Cost of New Medications*

- Sofosbuvir x 12 weeks: $84,000
- Sofosbuvir x 24 weeks: $168,000
- Simeprevir x 12 weeks: $66,360
- Sofosbuvir + Simeprevir x 12 weeks: $150,360

* Using Manufacturer’s Retail Price
On the Horizon

Drugs expected to be approved by the FDA by end of 2014
Interferon-Free Treatment for Genotype 1

Ledipasvir-Sofosbuvir Fixed Dose Combo (1 pill once/day)/Gilead – FDA approval expected by Oct 10, 2014

Expect FDA Approval October-December 2014:

- Daclatasvir-Asunaprevir/Bristol Meyers Squibb
- 3D Regimen/Abbvie
- Combining Simeprevir with Sofosbuvir/Janssen

Supplemental New Drug Application

Raising the Bar:
≥ 95% Cure Rates For All In the Future
Benefits of Hepatitis C Treatment

- Sustained virologic response (SVR) results in a 90% reduction in cirrhosis and 70% reduction in liver cancer \(^1,^2,^3\)

Hepatitis C Treatment Coverage

**Medicare Part D**
Obtain prior authorization

**AK Medicaid**
Covers *F3-F4 Fibrosis Only

**AK Marketplace Insurance Plans**
Moda, Premera
Cover *F3-F4 Fibrosis Only

**Private Insurance**
Obtain Prior Authorization

**Uninsured**
Send to Gilead Support Path (Sof)/Janssen Patient Assistance (Sim)

*F3-F4 Fibrosis = Advanced fibrosis of the liver (bridging fibrosis or cirrhosis)*
Treatment Reimbursement

- Write Rx, start prior authorization process for persons with insurance coverage
- Uninsured and Those Denied Coverage from Insurance

  - Contact Gilead Support Path (Sofosbuvir)
    - 1-855-7-MYPATH (1-855-769-7284)
    - SOVALDI.com/support

  - Janssen Prescription Assistance (Simeprevir)
    - 1-855-5-OLYSIO (1-855-565-9746)
    - janssenprescriptionassistance.com
Updated AASLD/IDSA Recommendations for Testing, Managing and Treating Hepatitis C

August 11, 2014 revision included new section:

In Whom and When to Initiate Treatment
“...clinicians should treat HCV-infected patients with antiviral therapy with the goal of achieving SVR, preferably early in the course of their chronic HCV infection before the development of severe liver disease and other complications.”

“Limitations of workforce and societal resources may limit the feasibility of treating all patients within a short period of time. Therefore, when such limitations exist, initiation of therapy should be prioritized first to those specific populations that will derive the most benefit or have the greatest impact on further HCV transmission. Others should be treated as resources allow.”

http://hcv.guidelines.org
## Grading System

<table>
<thead>
<tr>
<th>Classification</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class I</td>
<td>Conditions for which there is evidence and/or general agreement that a given diagnostic evaluation, procedure, or treatment is beneficial, useful, and effective</td>
</tr>
<tr>
<td>Class II</td>
<td>Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness and efficacy of a diagnostic evaluation, procedure, or treatment</td>
</tr>
<tr>
<td>Class IIa</td>
<td>Weight of evidence and/or opinion is in favor of usefulness and efficacy</td>
</tr>
<tr>
<td>Class IIb</td>
<td>Usefulness and efficacy are less well established by evidence and/or opinion</td>
</tr>
<tr>
<td>Class III</td>
<td>Conditions for which there is evidence and/or general agreement that a diagnostic evaluation, procedure, or treatment is not useful and effective or if it in some cases may be harmful</td>
</tr>
</tbody>
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<table>
<thead>
<tr>
<th>Level of Evidence</th>
<th>Description</th>
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<tbody>
<tr>
<td>Level A</td>
<td>Data derived from multiple randomized clinical trials or meta-analyses</td>
</tr>
<tr>
<td>Level B</td>
<td>Data derived from a single randomized trial, or nonrandomized studies</td>
</tr>
<tr>
<td>Level C</td>
<td>Consensus opinion of experts, case studies, or standard of care</td>
</tr>
</tbody>
</table>

Adapted from the American College of Cardiology and the AHA Practice Guidelines
When and in Whom to Initiate HCV Treatment

The goal of treatment is to reduce all-cause mortality and liver-related health adverse consequences, including ESLD and HCC, by the achievement of SVR (Class I, Level A).

Treatment is recommended for patients with chronic HCV infection (Class I, Level A)

- Treatment is assigned the highest priority for patients with advanced fibrosis, compensated cirrhosis, or severe extrahepatic HCV, and for LT recipients.
- Based on available resources, treatment should be prioritized as necessary so that patients at high risk for liver-related complications and severe extrahepatic complications are given high priority.

http://hcv.guidelines.org
Complications and Extrahepatic Disease Where Treatment is Most Likely to Provide the Most Immediate and Impactful Benefits

Highest Priority for Treatment Owing to Highest Risk for Severe Complications

<table>
<thead>
<tr>
<th>Complication</th>
<th>Class</th>
<th>Level</th>
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</thead>
<tbody>
<tr>
<td>Advanced fibrosis (Metavir F3) or compensated cirrhosis (Metavir F4) (Class I, Level A)</td>
<td></td>
<td></td>
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<tr>
<td>Organ transplant (Class I, Level B)</td>
<td></td>
<td></td>
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<tr>
<td>Type 2 or 3 essential mixed cryoglobulinemia with end-organ manifestations (eg, vasculitis) (Class I, Level B)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proteinuria, nephrotic syndrome, or membranoproliferative glomerulonephritis (MPGN) (Class IIa, Level B)</td>
<td></td>
<td></td>
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</table>

http://hcv.guidelines.org
Complications and Extrahepatic Disease Where Treatment is Most Likely to Provide the Most Immediate and Impactful Benefits

<table>
<thead>
<tr>
<th>High Priority for Treatment Owing to High Risk for Complications</th>
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<tbody>
<tr>
<td>Fibrosis (Metavir F2) (Class 1, Level B)</td>
</tr>
<tr>
<td>HIV-1 coinfection (Class 1, Level B)</td>
</tr>
<tr>
<td>Hepatitis B virus (HBV) coinfection (Class IIa, Level C)</td>
</tr>
<tr>
<td>Other coexistent liver disease (eg, [NASH]) Class IIa, Level C</td>
</tr>
<tr>
<td>Debilitating fatigue (Class IIa, Level B)</td>
</tr>
<tr>
<td>Type 2 diabetes mellitus (insulin resistant) (Class IIa, Level B)</td>
</tr>
<tr>
<td>Porphyria cutanea tarda (Class IIb, Level C)</td>
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“Successful treatment of HCV-infected persons at greatest risk for transmission represents a formidable tool to help stop HCV transmission in those who continue to engage in high-risk behaviors. To guide implementation of hepatitis C treatment as a prevention strategy, studies are needed to define the best candidates for treatment to stop transmission, the additional interventions needed to maximize the benefits of HCV treatment (e.g., preventing reinfection), and the cost effectiveness of the strategies when used in the target population.”
Persons Whose Risk of HCV Transmission is High and in Whom HCV Treatment May Yield Transmission Reduction Benefits

<table>
<thead>
<tr>
<th>High HCV Transmission Risk*</th>
</tr>
</thead>
<tbody>
<tr>
<td>MSM with high-risk sexual practices</td>
</tr>
<tr>
<td>Active IDUs</td>
</tr>
<tr>
<td>Incarcerated persons</td>
</tr>
<tr>
<td>Persons on long-term hemodialysis</td>
</tr>
<tr>
<td>(Rating: Class IIa, Level C)</td>
</tr>
</tbody>
</table>

*Patients at high risk of transmitting HCV should be counseled on ways to decrease transmission and minimize the risk of reinfection

http://hcv.guidelines.org
Populations Unlikely To Benefit from HCV Treatment

- Limited life expectancy (< 12 months) where treatment would not improve symptoms or prognosis
Articles on Hepatitis C Treatment Issues

- Researchers: Sovaldi Analysis Could Be Used In Lawsuits Against Medicaid. Inside CMS (online); 9/25/14.
Visit ANTHC Liver Disease & Hepatitis Program Website – Treatment Page

http://www.anthctoday.org/community/hep/providers/treatment/index.html
Special Thanks!!!

- Maggie Shuhart, MD University of Washington/Project Echo
- HCV advocates for keeping us all informed & pushing us to do more, including:
  - Ronni Marks, HepatitisCMsg.Org
  - Michael Ninburg, HepEducation.org
  - Jules Levin, Natap.org
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