An Update on Hepatitis C in the United States
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Therapy for Hepatitis C Saves Lives: Everyone Should Be Treated

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Disclosures
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- **Research Grants:**
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BOX 1-1
10 Leading Causes of Death Worldwide*

1. Ischemic heart disease
2. Cerebrovascular disease
3. Chronic Obstructive Pulmonary Disease
4. Lower respiratory infections
5. Alzheimer’s disease
6. Lung cancer
7. Viral hepatitis
8. Road injuries
9. HIV and AIDS
10. Diabetes

* Based on 2013 data.
SOURCES: Cooke et al., 2013; IHME, 2015; WHO, 2016a.
Increased Morbidity and Mortality Due to HCV Now and in the Future: U.S.

**Mortality Rates of HBV, HCV and HIV: 1999-2007**

- **HIV**
- **HCV**
- **HBV**

- By 2007 hepatitis C-associated deaths had overtaken HIV as a cause of mortality in the United States.
- New policies and commitments to detect and link infected persons to care and successful treatment are needed.

**Morbidity and Mortality Predictions**

- **DEATHS**
- ** Decompensation**
- **HCC**
- **TRANSPLANTS**

Hepatitis C May Progress to Cirrhosis and Liver Cancer

Normal Liver

Liver Cancer

CIRRHOSIS
Curing Hepatitis C Infection: Sustained Virological Response

SVR = CURE OF HCV INFECTION

HCV RNA

Baseline  Treatment  Follow-up

HCV RNA Undetectable

12 weeks Post-Treatment

Weeks

0  12  24
Mortality and Morbidity Reduced with HCV Cure

- 530 adults in Europe prospectively followed for median 8.4 years after HCV treatment
- 192 (36%) achieved SVR

**Adjusted HR of SVR:**
- Liver Failure: 0.07 (95% CI 0.03-0.20) \( p < 0.001 \)
- HCC: 0.19 (95% CI 0.08-0.44) \( p < 0.001 \)

**Cumulative Mortality**
- 30 adults in Europe prospectively followed for median 8.4 years after HCV treatment
- 192 (36%) achieved SVR

**Van der Meer JAMA 2012**
Decreased Five-year Mortality Rates in Multiple Populations Associated with SVR (Meta-analysis)

Simmons B et al, 2015 (epub)

General: 18 studies
n=29,269
Avg. FU = 4.6 years

Cirrhosis: 9 studies
n=2,734
Avg. FU = 6.6 years

HIV/HCV: 5 studies
n=2,560
Avg. FU = 5.1 years

General= Studies that include all stages of liver disease

<table>
<thead>
<tr>
<th>Group</th>
<th>Studies</th>
<th>n</th>
<th>Avg. FU (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>General</td>
<td>18</td>
<td>29,269</td>
<td>4.6</td>
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<td>HIV/HCV</td>
<td>5</td>
<td>2,560</td>
<td>5.1</td>
</tr>
</tbody>
</table>

Mortality %

- General: 2%
- Cirrhosis: 7.8%
- Co-infected: 11.4%

Simmons B et al, 2015 (epub)
Curing Hepatitis C Has Myriad Benefits

Decreased Liver Inflammation

Decreased Liver Scarring

Stops Disease Progression

Decreased Liver Transplantation

Decrease Rate of Liver Cancer

Resolves Stigma

Improved Quality of Life

Improvement in All-Cause Mortality

Adapted from Ford et al, 2015
Significant Advances Have Been Achieved for the Treatment of Chronic HCV Infection

- Fatigue, Flu-like symptoms
- Anxiety, Depression
- Anemia, Low WBC
- Few candidates due to comorbidities
- Numerous treatment discontinuations

**1991**
Interferon
16%

**1998**
IFN/RBV
35%

**2001**
PegIFN/RBV
44%

**2011**
Telaprevir* or Boceprevir + PegIFN/RBV
~70%

**2013-2016**
2nd Generation DAAs
>90%

Fried et al, 2002
Schaefer EA et al., 2012;

*Telaprevir and boceprevir no longer sold in U.S. October 16, 2014.
Combination Therapies in 2016

Protease inhibitors
- Simeprevir
- Paritaprevir
- Grazoprevir

NS5A Inhibitors
- Ledipasvir
- Elbasvir
- Daclatasvir
- Ombitasvir

NS5B Nucs
- Sofosbuvir

NS5B Non-nucs
- Dasabuvir

DAA Regimens in Use

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Direct Acting Antiviral Class</th>
</tr>
</thead>
<tbody>
<tr>
<td>HARVONI: Sofosbuvir + Ledipasvir</td>
<td>NUC + NS5A</td>
</tr>
<tr>
<td>VIEKIRA-Pak: Paritaprevir + Ombitasvir + Dasabuvir +/- RBV</td>
<td>PI + NS5A + NNI</td>
</tr>
<tr>
<td>ZEPATIER: Grazoprevir + Elbasvir</td>
<td>PI + NS5A</td>
</tr>
<tr>
<td>EPCLUSA: Sofosbuvir + Velpatasvir</td>
<td>NUC + NS5A</td>
</tr>
<tr>
<td>Sovaldi+ Dakilinza</td>
<td>NUC + NS5A</td>
</tr>
</tbody>
</table>
Treatments Are Simple and Have Almost No Side Effects
Rates of SVR (CURE) are High Across All Regimens HCV Genotype 1 Treatment Naive

- **Sofosbuvir Ledipasvir**
- **Paritaprevir/r Ombitasvir Dasabuvir +/-RBV**
- **Grazoprevir Elbasvir**
- **Sofosbuvir Daclatasvir**

TN G1, TN G1 No Cirrhosis, TN G1 Cirrhosis
The Cascade of Care has improved in the DAA era but more must be done. Currently available therapies can cure almost everyone. Access to Care remains the greatest barrier to control of HCV.
Access to Care: Case 1

• 56 y/o man who injected drugs until 1980
  – Married, one daughter age 23
  – Insured by Medicaid
  – Asymptomatic, ALT= 37
  – Advanced fibrosis: F3: (Increased risk for liver cancer and progression to cirrhosis)

• This patient would be eligible for treatment in all of these cities except:
  – Miami Beach
  – Baltimore
  – Chapel Hill, North Carolina
  – Chicago, Illinois
Access to Care: Case 2

- 26 y/o woman previously addicted to prescription drugs and then heroin
  - Completed drug rehab program in 2012
  - State health insurance
  - Married, one daughter age 3
  - Recently graduated from college
  - Mild fatigue, ALT= 37
  - Mild fibrosis: Stage F1

- This patient would be eligible for treatment if she lived in which of these cities:
  - Detroit
  - Chapel Hill, NC
  - Miami Beach
  - Los Angeles
Inconsistent Restrictions in State Medicaid Reimbursement for HCV Therapy

- 32 States require evidence of moderate or advanced scarring of the liver
- (Advanced scarring already increases risk for liver cancer)

- Majority of state insurance plans require a defined period of abstinence from alcohol and/or drugs
- Some states require drug testing for all treatment candidates

Barua et al, 2015
Prior Authorizations for Treatment in North Carolina: Frequent Denials

Patients Prescribed HCV Medications
(10/2014 - 4/2016)

n = 1017 (%)

- Initially Approved: 794 (78.1%)
- Pending: 4 (0.4%)
- Initially Denied: 206 (20.2%)
- Appealed: 146 (70.9%)
  - Approved: 115 (78.8%)
  - Pending: 9 (6.1%)
  - Denied: 22 (15.1%)
- Closed: 13 (1.3%)
  - Did not Appeal: 60 (29.1%)
  - Closed: 4 (18.2%)

Reasons for Denial

<table>
<thead>
<tr>
<th>Reason</th>
<th>Count (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;F2 Fibrosis</td>
<td>65 (31.6%)</td>
</tr>
<tr>
<td>Did Not Meet Criteria</td>
<td>57 (27.7%)</td>
</tr>
<tr>
<td>Non-Formulary/Plan Exclusion</td>
<td>41 (19.9%)</td>
</tr>
<tr>
<td>Missing Information</td>
<td>20 (9.7%)</td>
</tr>
<tr>
<td>Others**</td>
<td>23 (11.1%)</td>
</tr>
</tbody>
</table>

- Medicare: Highest approval rate
- Medicaid: Lowest approval rate and fewest successful appeals

*Others: <F3 Fibrosis (7), Genotype (6), Partial Duration (8), Need to apply for insurance (2)

Giang et al, unpublished
Therapy for Hepatitis C Saves Lives: Everyone Should Be Treated

- The burden of hepatitis C is immense and often underestimated
- Curing hepatitis C will have a positive impact by:
  - Decreasing the incidence of cirrhosis
  - Decreasing hepatocellular carcinoma
  - Improving overall quality of life for patients with HCV
- Multiple barriers exist that arbitrarily restrict access to all who would benefit from HCV cure
- We must continue to be the champions to effect change and to shape policies that will lead to greater access to care for all patients
Thank you!