HCV: Racial Disparities

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Charles Howell Disclosures

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  - Boehringer Ingelheim, Inc.
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  - Gilead Sciences, Inc.

- **Advisory Boards**
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  - Janssen, Inc.
  - Vertex, Inc.
Hepatitis C Virus (HCV) in US

- 4 million infected with HCV (NHANES 1999-2002)
- 3 million with chronic HCV (viremia)
- Most common blood-borne viral infection
- Leading cause for cirrhosis & primary hepatocellular carcinoma (HCC)
- Indication for ~50% of liver transplants

Natural History of HCV Infection

15% Resolved
85% Chronic

20% Cirrhosis

~20 year progression rate accelerated with HIV, HBV, alcohol

6%/yr ESLD
4%/yr HCC
3-4%/yr Transplant/death

5-year survival in patients with HCC is <5%

HCC = hepatocellular carcinoma
ESLD = end-stage liver disease
Factors Associated with Fibrosis in HCV

- Age at infection
- Duration of infection
- Metabolic factors (steatosis, obesity, diabetes)
- Compromised immune system
- Genetic factors
- HIV co-infection
- HBV co-infection
- Heavy alcohol use

NHANES III Demographic Characteristics of Persons Infected with HCV Genotypes 1, 2, and 3

Nainan OV et al. *Hepatology* 2005:42(suppl 1):660A.
Greater HCV Burden in African Americans (AA)

- HCV twice as prevalent in AA vs. Caucasian (CA) or White (3.0% vs. 1.5%)
- Race and Ethnicity (NHANES 1999-2002):
  - 2.6 million CA (65%)
  - 920,000 AA infected with HCV (23%)
  - 260,000 Mexican Americans (6.5%)
- AA: 12-13% of US pop. & 23% of HCV cases
- 9% of AA 40-49 years old infected compared to 3.8% of CA
- Estimate 1-2 million AA infected (higher incarceration and homeless rates)

Trends in HCC Incidence in US

NCI SEER Data

Per 100,000 Population

Annual Hepatitis C Mortality Rates:
Race/Ethnicity

Mortality Rate from HCV Exceeds that of HIV

Ly et al. AIM 156:271-278, 2012
HCV-related Deaths in 2007

- 73.4% Age 45-59
  - 45-54 39%
  - 55-64 34%
- 70% Males [OR 2.4  95% CI (2.3-2.4)]
- 18% Non-Hispanic Black [OR 1.9 (1.8-2.0)]
- 15% Hispanic [OR 3.4 (3.2-3.50)]
- 2.9% HIV Co-infection [OR 5.8 (5.3-6.4)]
- 3.6% HBV Co-infection [OR 70.3 (63.5-77)]
- 57.2% Chronic Liver Disease [OR 57 (55-59)]
- 19.4% Alcohol-related condition [OR 13 (12.8-14)]

Ly et al. AIM 156:271-278, 2012
Aging of HCV-Infected Persons in the US: Disease Progression

Projected Prevalence of Chronic HCV, Cirrhosis, and Complications

Projected Number of Patients With Decompensated Cirrhosis and Hepatocellular Carcinoma

HCV Cured by Treatment: Sustained Virological Response (SVR)

- Tantamount to cure; HCV RNA remains negative in 99%
- Associated with improvement in liver histology (inflammation, fibrosis)
- Less frequent liver-related complications
- Reduced risk of liver decompensation
- Reduced risk of hepatocellular carcinoma
- Reduced liver-related mortality

Milestones in Therapy of HCV: Overall SVR Rates

Average SVR Rates from Clinical Trials

<table>
<thead>
<tr>
<th>Year</th>
<th>IFN 6m</th>
<th>IFN 12m</th>
<th>IFN/RBV 6m</th>
<th>IFN/RBV 12m</th>
<th>Peg-IFN 12m</th>
<th>Peg-IFN/RBV 12m</th>
<th>Telaprevir PR24/48</th>
<th>P/R/B (48 wk) + lead-in</th>
</tr>
</thead>
<tbody>
<tr>
<td>1991</td>
<td>6%</td>
<td>16%</td>
<td>34%</td>
<td>42%</td>
<td>39%</td>
<td>54-56%</td>
<td>79%*</td>
<td>68%*</td>
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<td>1999</td>
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<td>2002</td>
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<td>2010</td>
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*Data from genotype 1 patients

Screening and Diagnosis
In the US, 2.7–3.9 million people are living with chronic HCV infection; 75% are unaware they are infected.

- Goal: diagnosis before advanced fibrosis/cirrhosis when treatment more effective and beneficial
- Screen at risk groups for anti-HCV
  - Abnormal ALT
  - History of past or current Injection Drug Use
  - Chronic hemodialysis
  - Recipients of clotting factors before 1987
  - Recipients of transfusion or organ transplant prior to July 1992
  - Needle stick or mucosal exposure to HCV+ blood
  - Children of HCV+ mothers
  - Sexual partners of HCV+ (AASLD)
- Enzyme Immunoassay (EIA) 3.0: sensitivity 97-99% & positive predictive value 98-99% in high prevalence groups
  
  
New 2012 Recommendations—Individuals Who Should Be Screened for HCV

Baby Boomers Born from 1945–1965

- Adults born during 1945–1965 should receive one-time testing for HCV without prior ascertainment of HCV risk

- As of 2012, this includes all individuals between 47 and 67 years of age!
Three-fourths Chronic HCV in the US Were Born Between 1945 and 1965

Estimated Prevalence by Age Group

New 2012 Recommendations—Individuals Who Should Be Screened for HCV

- IDU
- Clotting factors made before 1987
- Received blood/organs before July 1992
- Hemodialysis
- Elevated alanine aminotransferase [ALT] levels
- HIV

Testing also should be performed based on the need for exposure management, including:

- Health care, emergency, and public safety workers after needlestick/mucosal exposure to HCV-positive blood
- Children born to HCV-positive women

New 2012 Recommendations—Reduce Alcohol Use in Patients with HCV

- All persons with identified HCV infection should receive brief alcohol screening, brief counseling if positive, followed by referral to appropriate care and treatment services.

- Screening tools:
  - National Institute on Alcohol Abuse and Alcoholism
  - WHO


Barriers to Healthcare: Access

- Access (e.g., insurance status, ability to pay for healthcare) most important predictor of the quality of healthcare across racial and ethnic groups (*IOM: Unequal Treatment*)
- Black Americans twice as likely to have no private health insurance
- Latina American 3 times less likely to have private health insurance
- Affordable Care Act 2010 access for 60% (~30 million) of uninsured
Barriers to Healthcare: Patient & Provider Knowledge

- AA, older age, and < high school education less knowledgeable about HCV
- Low rate of HCV risk factor documented in primary care clinics
  - IDU-12%
  - Blood transfusion before ‘92-2%
- Minorities with a HCV risk factor less likely to receive testing (23% vs 35%, P = 0.004)

Disparities in HCV Treatment: Peginterferon & Ribavirin

- AA & Hispanics less likely to be treatment candidate according to clinicians
- AA and Hispanics receive fewer interferon prescriptions for HCV
- AA more likely to decline treatment (did not explain the disparity)
- Provider & facility factors have larger effect on variability in treatment than patient factors

HCV Screening in Minorities

- Outcomes and impact of new HCV screening on future liver-related morbidity and mortality need to be closely monitored
  - Less access to health care and other barriers to risk-based screening and treatment
  - Identify and distribute best practices
  - Broad community-based screening; not limited to physician offices
  - Referral to care and treatment
Treatment Considerations
## 2 Protease Inhibitors (PIs)
Approved for HCV Genotype 1

<table>
<thead>
<tr>
<th>Protease Inhibitor</th>
<th>Additional Regimen Components</th>
<th>Considerations</th>
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<tbody>
<tr>
<td>Boceprevir 800 mg TID (q7-9hrs)(^1,2)</td>
<td>PEG-IFN alfa + weight-based RBV</td>
<td>▪ Naïve to previous therapy&lt;br&gt;▪ Previous treatment failure&lt;br&gt;▪ Compensated cirrhosis&lt;br&gt;▪ Response-guided therapy (RGT)</td>
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For patients with genotype 2/3 infection, HCV therapy with PEG-IFN/RBV remains the standard of care (SVRs-75-82%)

Boceprevir: Treatment Naïve Patients
SVR and Race

Non-Black/African-American

- **BOC**: boceprevir 800 mg q8h
- **PR**: PegIFN α-2b 1.5 µg/kg/wk + weight-based RBV 600-1400 mg/day

<table>
<thead>
<tr>
<th>Group</th>
<th>Percent of Patients</th>
<th>N</th>
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<tbody>
<tr>
<td>PR48 n = 311</td>
<td>40</td>
<td></td>
</tr>
<tr>
<td>RGT n = 316</td>
<td>67</td>
<td></td>
</tr>
<tr>
<td>BOC/PR48 n = 311</td>
<td>68</td>
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Black/African American

<table>
<thead>
<tr>
<th>Group</th>
<th>Percent of Patients</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>PR48 n = 52</td>
<td>23</td>
<td></td>
</tr>
<tr>
<td>RGT n = 52</td>
<td>42</td>
<td></td>
</tr>
<tr>
<td>BOC/PR48 n = 55</td>
<td>53</td>
<td></td>
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</tbody>
</table>

**P-values**
- $P < 0.0001$
- $P < 0.0001$
- $P < 0.004$
- $P < 0.044$

Telaprevir: Treatment Naïve Patients
SVR Rates by Race or Ethnicity

TVR: Telaprevir 750 mg q8h; PR: PegIFN α -2a 180 µg/wk + weight-based RBV 1000-1200 mg/day; Pbo: placebo

FDA Antiviral Drugs Advisory Committee.
HCV Genome & Gene Products: Potential Targets for Direct Acting Antiviral Agents (Present & Future)

Protease Inhibitors: boceprevir; telaprevir

The Future: Various Paradigms Being Developed Simultaneously

- Interferon-free regimens
- PR + single DAA
  - PIs
  - Nucleoside analogs
  - NS5A Inhibitors
- “Quad”
  - PR + DAA-1 + DAA-2
Under-representation in HCV Clinical Trials

- Few minorities enrolled in clinical trials 1989-2002;
- 2004-2006: 3 clinical trials of peginterferon & ribavirin for HCV genotype 1 in AA
- 2009: 1st clinical trial of peginterferon & ribavirin for HCV genotype 1 in Latino Whites
- AA and Latinos poorly represented in direct acting antiviral clinical trials
- Increased participation in clinical trials necessary
  - improve efficacy of therapy in AA
  - evidence-based management