The Intersection of HIV and Hepatitis C

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Major Historical Milestones in HIV and HCV

**HIV**
- Causal organism isolated
- First description of P. carinii cluster
- First serum assay approved
- First treatment approved
- Combination antiviral therapy

**Hepatitis C**
- First description of non A non B hepatitis
- Causal organism isolated and cloned
- First treatment approved
- First serum assay approved
- Combination antiviral therapy

Curran, MMWR 2011; Center for Disease Control Viral Hepatitis Fact Sheet
Viral Characteristics

- **Retrovirus**
- Double stranded
- RNA $\rightarrow$ DNA $\rightarrow$ RNA

- **Flavivirus**
- Single stranded, positive sense
- RNA $\rightarrow$ RNA
<table>
<thead>
<tr>
<th></th>
<th>HIV</th>
<th>Hepatitis C</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Target Host Cell</strong></td>
<td>CD4+ T Cell</td>
<td>Hepatocyte</td>
</tr>
<tr>
<td><strong>Replication</strong></td>
<td>Latent</td>
<td>Active</td>
</tr>
<tr>
<td><strong>Population</strong></td>
<td>1 million</td>
<td>5 million</td>
</tr>
<tr>
<td><strong>Mutation Rates</strong></td>
<td>Very high</td>
<td>Very high</td>
</tr>
<tr>
<td><strong>Virions/Day</strong></td>
<td>$10^{10}$</td>
<td>$10^{12}$</td>
</tr>
<tr>
<td><strong>Genetic Archive</strong></td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

Adapted from Soriano et al, JAC 2008
## Current Directly Acting Antivirals

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Genotypes</th>
<th>Duration</th>
<th>SVR (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SOF/RBV</td>
<td>ALL</td>
<td>12-24 WKS</td>
<td>70-100</td>
</tr>
<tr>
<td>LDV/SOF</td>
<td>1 &amp; 4</td>
<td>12-24 WKS#</td>
<td>&gt;95</td>
</tr>
<tr>
<td>SOF/VEL</td>
<td>ALL</td>
<td>12 WKS#</td>
<td>&gt;99</td>
</tr>
<tr>
<td>DAC/SOF</td>
<td>ALL</td>
<td>12-24 WKS#</td>
<td>&gt;95</td>
</tr>
<tr>
<td>PRO-D/TECHNIVIE@</td>
<td>1 &amp; 4</td>
<td>12-24 WKS</td>
<td>&gt;90</td>
</tr>
<tr>
<td>GRZ/ELB</td>
<td>1 &amp; 4</td>
<td>12-16 WKS$</td>
<td>&gt;95</td>
</tr>
</tbody>
</table>

# RBV to be added for decompensated cirrhosis
@Dasabuvir has no activity against genotype 4
$ RBV to be added for those with baseline NS5A mutations

AASLD-IDSA HCV Guidance (hcvguidance.org)
Hepatitis C Care Continuum

Adapted from Yehia et al PLOS One 2015
Where does the HCV field go from here?
Dramatic Progress in HIV Treatment

Towards and Beyond 2015: Rapid Progress and New Horizons in HIV Treatment

Progress

4.2 million lives saved through ART\(^*\) scale up

Global target for 15 million people on ART by 2015 is achievable

9.7 million on ART at the end of 2012

1.6 million more people on ART in 2012. Largest annual increase ever

* (ART = antiretroviral therapy)

All statistics can be found in Global update on HIV treatment 2013: Results, impact and opportunities and WHO Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection (June 2013), found here: http://www.who.int/hiv
Key Factors in HIV Treatment Implementation

Scientific Advancements

- Combination ART
- Refined Technical Approach
- Rapid Diagnostic Testing
Key Factors in HIV Treatment Implementation
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Hepatitis C Care Continuum

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HCV Treatment Implementation

Scientific Advancements

- Combination DAA Therapy
- Refined Technical Approach
- Rapid Diagnostic Testing

Algorithm-based
- Minimal lab monitoring
- Task Shifting
- Incorporating care into existing settings
- Use of generics

NIH ASCEND Investigation
Study Design

- Two urban health systems
- 16 providers
  - 5 NP
  - 5 PCP
  - 6 Specialist (ID/Hepatology)
- Uniform 3-hour training

Kattakuzhy, Annals of Internal Medicine 2017
Methods

• No study team involvement after initial visit

• Standardized visit schedule based on AASLD-IDSA guidance
  • Monthly provider visits
  • Week 4 safety labs
  • HCV viral load testing at week 4 and SVR12
Primary Outcome

Percentage with SVR

- NP: 89.4% (135/151)
- PCP: 86.3% (138/160)
- Specialist: 83.0% (240/289)
- Overall: 85.5% (513/600)

$p=0.19$
HCV Treatment Implementation

- Scientific Advancements
  - Combination DAA Therapy
  - Refined Technical Approach
  - Rapid Diagnostic Testing

- Algorithm-based
- Minimal lab monitoring
- Task Shifting
- Incorporating care into existing settings
- Use of generics
HCV Medication Cost

<table>
<thead>
<tr>
<th>Medication</th>
<th>Trade Name</th>
<th>Manufacturer</th>
<th>WAC for 1 Day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daclatasvir</td>
<td>Daklinza</td>
<td>Bristol-Myers Squibb</td>
<td>$750</td>
</tr>
<tr>
<td>Elbasvir-Grazoprevir</td>
<td>Zepatier</td>
<td>Merck &amp; Co., Inc.</td>
<td>$650</td>
</tr>
<tr>
<td>Ledipasvir-Sofosbuvir</td>
<td>Harvoni</td>
<td>Gilead Sciences</td>
<td>$1125</td>
</tr>
<tr>
<td>Glecaprevir-Pibrentasvir</td>
<td>Mavyret</td>
<td>AbbVie</td>
<td>$417</td>
</tr>
<tr>
<td>Ombitasvir-Paritaprevir-Ritonavir</td>
<td>Technivie</td>
<td>AbbVie</td>
<td>$912</td>
</tr>
<tr>
<td>Ombitasvir-Paritaprevir-Ritonavir and Dasabuvir</td>
<td>Viekira Pak</td>
<td>AbbVie</td>
<td>$992</td>
</tr>
<tr>
<td>Simeprevir</td>
<td>Olysio</td>
<td>Janssen</td>
<td>$790</td>
</tr>
<tr>
<td>Sofosbuvir</td>
<td>Sovaldi</td>
<td>Gilead Sciences</td>
<td>$1000</td>
</tr>
<tr>
<td>Sofosbuvir-Velpatasvir</td>
<td>Epclusa</td>
<td>Gilead Sciences</td>
<td>$890</td>
</tr>
<tr>
<td>Sofosbuvir-Velpatasvir-Voxilaprevir</td>
<td>Vosevi</td>
<td>Gilead Sciences</td>
<td>$890</td>
</tr>
</tbody>
</table>

**Figure 2 - Wholesale Acquisition Cost versus Estimated Production Cost for DAAs and 12-Week Treatment Course**

### HCV Generics

- Gilead License Agreements
- Emerging observational data that licensed generics have equal efficacy

<table>
<thead>
<tr>
<th>Viral status</th>
<th>Overall n/total n (%)</th>
<th>SOF/LDV n/total n (%)</th>
<th>SOF/DCV n/total n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SVR 12</td>
<td>247/250(99)</td>
<td>104/104(100)</td>
<td>143/146(98)</td>
</tr>
<tr>
<td>SVR 24</td>
<td>96/97(99)</td>
<td>30/30(100)</td>
<td>66/67(99)</td>
</tr>
</tbody>
</table>

Hill et al, J Virus Erad 2017
Limited Advocacy

- Delayed serious outcomes reduce urgency
- Unequal access to medications
- Disenfranchised populations excluded

Younossi et al, J Viral Hepat 2016
Limited Government Investment

- Research Funding on HCV is tied to subgroups of political interest, not to disease or implementation needs.

- Senate Finance Committee inquiry into Sovaldi pricing December 2015 did not lead to significant price changes.

- No PEPFAR or RWCA equivalents.

- Medicaid coverage varies state to state and includes non-evidence based restrictions on liver fibrosis stage, substance use, and provider type.

Barua et al, Annals 2015
Where does the HCV field go from here?

- Refine our technical approach through large scale, randomized implementation studies
- Increase advocacy, engaging marginalized populations
- Gain government buy-in
- Obtain access to generic medications
Thank You

Office of AIDS Research

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• Angie Price NP

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• Chloe Gross RN
• Elizabeth Akoth RN
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• Poonam Mathur DO

Community Partners
• Unity Healthcare
• Family Medical Counseling Services
• HIPS
• RAP
• DC DOH
• WWH

Patients of the District of Columbia
# Clinical Characteristics

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<thead>
<tr>
<th></th>
<th>HIV</th>
<th>Hepatitis C</th>
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<tbody>
<tr>
<td><strong>Transmission</strong></td>
<td>Blood, Sex, Mother to Child</td>
<td>Blood, Sex, Mother to Child</td>
</tr>
<tr>
<td><strong>Progression</strong></td>
<td>Slow, ~10 years to fatal disease</td>
<td>Slow, ~20 years to fatal disease in some</td>
</tr>
<tr>
<td><strong>Mortality</strong></td>
<td>High in nearly all infected patients if untreated</td>
<td>High in advanced fibrosis patients if untreated</td>
</tr>
<tr>
<td><strong>Drug Targets</strong></td>
<td>Multiple</td>
<td>Multiple</td>
</tr>
<tr>
<td><strong>Therapy Duration</strong></td>
<td>Lifelong</td>
<td>8-24 weeks</td>
</tr>
<tr>
<td><strong>Current Therapeutic Goal</strong></td>
<td>Suppression</td>
<td>Eradication</td>
</tr>
</tbody>
</table>