Transformative Therapies for HCV: Paving the Way for HCV Elimination?

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Disclosures (past 12 months)

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Consultant/Advisor: nothing to disclose
Outline

1. Setting the stage for elimination
   1. HCV epi and defining elimination
   2. Recent advances in DAA therapy
   3. Will resistance derail elimination efforts?

2. Current status toward HCV elimination
   1. Global cascade and local examples
   2. Key populations going forward

HCV Elimination

CAN WE REALLY TREAT OUR WAY OUT OF THIS?
Global HCV Prevalence: 1.0% (71 million)

Prevalence (viremic)
- 0.0-0.1%
- 0.1-0.5%
- 0.5-0.8%
- 0.8-1.3%
- 1.3-2.9%
- >2.9%

USA
- Prevalence: 0.9% (0.7-1.2)
- Viremic (1000s): 2396 (2231-3826)

Global HCV Genotype Distribution
Elimination of Hepatitis C virus

**Elimination vs. Eradication**

- **Elimination** - reduction to 0 (or some low pre-defined threshold) in incidence/prevalence in a specific geographic region(s) through targeted and on-going interventions *(think polio)*

- **Eradication** - global, permanent reduction to 0 (incidence/prevalence) without the need for ongoing efforts *(think smallpox)*

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**WHO Global Hepatitis Elimination Strategy**

**2030 HCV Targets**

- **Diagnosis**: 90% diagnosed
- **Incidence**: 80% reduction
- **Treatment**: 80% treated
- **Mortality**: 65% reduction

What is it about HCV replication/life cycle that makes elimination possible?

HCV and HIV Replication Dynamics

*does not account for “curing” of infected hepatocytes
Intrahepatic viral decay during DAA therapy: A5335s

**Graph 1:**
- **Participants:** A, B, C, D, E
- **Biopsy 1:** 8 (4, 17)
- **Biopsy 2:** 12 (5, 27)

**Graph 2:**
- **Group:** All participants, Participants A-D
- **Overall Absolute Change:**
  - All participants: -24.6 [-41.4, -7.8]
  - Participants A-D: -19.4 [-33.2, -5.7]

**Intrahepatic viral decay during DAA therapy: A5335s**

**Graph 3:**
- **Estimated No. Infected Hepatocytes (log10 cells)**
- **Days after treatment initiation:** 0, 7, 14, 21, 28, 35, 42, 49, 56, 63, 70, 77
Key updates in DAA treatment

Shift in HCV Treatment Population

- Trio Health Survey
  - 19,944 patients
- 5 discrete 6 month time periods
  - DEC’13 (SOF+SMV)
  - DEC ‘17 (GLE/PIB)

No Bad Options

<table>
<thead>
<tr>
<th>Drug Regimen</th>
<th>Indications in Treatment-Naïve Adults w/o Cirrhosis</th>
<th>Duration of Treatment*</th>
</tr>
</thead>
<tbody>
<tr>
<td>EBR/GZR</td>
<td>GT1 or GT4; <strong>RAS testing in 1a limiting</strong></td>
<td>12 weeks</td>
</tr>
<tr>
<td>GLE/PIB</td>
<td>All genotypes</td>
<td>8 weeks</td>
</tr>
<tr>
<td>LDV/SOF</td>
<td>GT1, GT4, GT5, or GT6; Low VL (&lt;6 million) 8 week option; generic</td>
<td>8–12 weeks</td>
</tr>
<tr>
<td>SOF/VEL</td>
<td>All genotypes; generic</td>
<td>12 weeks</td>
</tr>
</tbody>
</table>

* Guidance recommended regimens; alternative durations in select scenarios but not recommended.

Lights out efficacy in the “real-world”

**MISTRAL Cohort (n=1177): GLE/PIB 8-12 weeks**
- GT1b: 37%, GT2: 35%; GT3 10%
- 90% 8 week duration
- GT3: 95% SVR (117/123)

**Puglia registry (n=1319): SOF/VEL 12 weeks**
- GT1: 40%, GT2: 39%; GT3 16%
- 7% of F3/F4 got RBV
- PWID: higher early D/C and LTFU
Simplified HCV Treatment Algorithm

- Treatment naïve, non-cirrhotic
  - Excluded HIV co-infection; +HBsAg
  - Limited fibrosis assessment
  - Streamlined pre-tx labs
    - No mandatory GT
- GLE/PIB x 8wks or SOF/VEL x 12wks
  - No routine on treatment monitoring
  - SVR12: HCV RNA and hepatic function
- Ongoing risks: at least annual HCV RNA

Role of RBV with VEL/SOF: GT3 with cirrhosis

English Registry (Drysdale K. EASL 2019)

<table>
<thead>
<tr>
<th>Comparison 2 (SVR12 in GT3 patients with compensated cirrhosis)</th>
<th>Comparator regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>SOF/VEL + RBV (12 weeks)</td>
<td>196</td>
</tr>
<tr>
<td>SOF/VEL</td>
<td>218</td>
</tr>
<tr>
<td>SOF + DCV + RBV</td>
<td>868</td>
</tr>
<tr>
<td>GLE/PIB (12 weeks)</td>
<td>167</td>
</tr>
</tbody>
</table>

Sofosbuvir/Velpatasvir 12 weeks
Relapse Rates 5%

Sofosbuvir/Velpatasvir + Ribavirin 12 weeks
Relapse Rates 2%
**Shortened Treatment for Uncomplicated Cirrhosis**

**Glecaprevir/Pibrentasvir**

- Cirrhosis ≥14.6 kPa (VCTE)
- Child-Pugh ≤6
  - PLT ≥ 50k
  - ALB ≥ 2.8mg/dL
  - TB ≤ 3mg/dL
- HIV-1 co-infection excluded

### Clinical characteristics

- 90% Child-Pugh A5
- 23.7 kPa mean
- PLT 152 (17% <100)
- ALB 4.2 (2.7-5.1)

No drug related SAEs or on treatment grade 2 or higher ALT/AST elevations

No VFs; 5 LTFU, 1 early D/C
Updated recommendation for treatment naïve patients with cirrhosis

Recommended regimens listed by evidence level and alphabetically for:
Treatment-Naïve Genotype 1a Patients With Compensated Cirrhosis

<table>
<thead>
<tr>
<th>Recommended</th>
<th>Duration</th>
<th>Rating</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily fixed-dose combination of elbasvir (50 mg)/grazoprevir (100 mg) for patients without baseline NS5A-RAs for elbasvir</td>
<td>12 weeks</td>
<td>I, A</td>
</tr>
<tr>
<td>Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg)</td>
<td>12 weeks</td>
<td>I, A</td>
</tr>
<tr>
<td>Daily fixed-dose combination of sofosbuvir (400 mg)/valpatasvir (100 mg)</td>
<td>12 weeks</td>
<td>I, A</td>
</tr>
<tr>
<td>Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg)</td>
<td>8 weeks</td>
<td>I, B</td>
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</tbody>
</table>

FDA approval of 8 week regimen in cirrhosis (9/26/19)

Could multi-drug resistant HCV Impact Elimination efforts?
Failure rates in registrational trials

<table>
<thead>
<tr>
<th>DAAs</th>
<th>Population</th>
<th>SVR</th>
<th>VF</th>
<th>Non-VF</th>
</tr>
</thead>
<tbody>
<tr>
<td>LDV/SOF (12wk)</td>
<td>GT1 TN GT1 TE GT4</td>
<td>99%</td>
<td>&lt;1%</td>
<td>&lt;1%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>94%</td>
<td>6%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>93%</td>
<td>7%</td>
<td></td>
</tr>
<tr>
<td>EBR/GZR (12wk)</td>
<td>GT1,4,6 TN GT1,4,6 TE</td>
<td>95%</td>
<td>4% (6% 1a)</td>
<td>1%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>92%</td>
<td>6%</td>
<td>2%</td>
</tr>
<tr>
<td>SOF/VEL (12wk)</td>
<td>GT1,2,4-6 GT 3</td>
<td>99%</td>
<td>&lt;1%</td>
<td>&lt;1%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>95%</td>
<td>4%</td>
<td></td>
</tr>
<tr>
<td>GLE/PIB (8wk)</td>
<td>GT1 NC GT3 NC GT5,6</td>
<td>99%</td>
<td>&lt;1%</td>
<td>&lt;1%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>95%</td>
<td>4%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>98%</td>
<td>2%</td>
<td></td>
</tr>
</tbody>
</table>

HCV Target cohort: Who is failing?

4099 GT1 patients treated with all-oral DAA regimens
- 259 (6.3%) failed therapy
Modeling the future burden of DAA failures

From 2014-2020 an estimated 47,000 DAA failures will be realized in Europe
- 33-52% of failure pts will be NS5A exposed (~25,000)
World 2.9 million DAA treatments 2015-2016 → 290,000 non-SVR
90% resistance: 261,000 DAA failures with resistance

WHO Progress Report on Access to Hepatitis C Treatment 2018

Image stolen from Chip Schooley
Rate of selection of NS5A resistance upon virologic failure

- Varies by regimen and duration
  - PI based
    - GZR/EBR: 94%
    - 3D: 68%
  - Nucleotide based
    - SOF/LDV: 75%
    - SOF/VEL: 93% (14/15; majority GT3)
  - Next generation regimens
    - SOF/VEL/VOX (8-12): 4-14%
    - G/P: 89%\(^5\)

\(^5\)9 failures out of 2256 treated

~75% of selected NS5A RASs are still present 3 years later

Improved resistance profile of “Next Generation” NS5As

<table>
<thead>
<tr>
<th>Fold Change</th>
<th>Genotype 1a</th>
<th>Genotype 1b</th>
<th>GT3a</th>
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<tbody>
<tr>
<td></td>
<td>M28T</td>
<td>Q30R</td>
<td>L31M/V</td>
</tr>
<tr>
<td>Ledipasvir</td>
<td>20x</td>
<td>&gt; 100x</td>
<td>&gt; 100x/ &gt; 100x</td>
</tr>
<tr>
<td>Ombitasvir</td>
<td>&gt; 1000x</td>
<td>&gt; 100x</td>
<td>&lt; 3x</td>
</tr>
<tr>
<td>Daclatasvir</td>
<td>&gt; 100x</td>
<td>&gt; 1000x</td>
<td>&gt; 100x/ &gt; 1000x</td>
</tr>
<tr>
<td>Elbasvir</td>
<td>20x</td>
<td>&gt; 100x</td>
<td>&gt; 10x</td>
</tr>
<tr>
<td>Velpatasvir</td>
<td>&lt; 10x</td>
<td>&lt; 3x</td>
<td>20x/50x</td>
</tr>
<tr>
<td>Pibrentasvir</td>
<td>&lt; 3x</td>
<td>&lt; 3x</td>
<td>&lt; 3x</td>
</tr>
</tbody>
</table>

Retreatment options for DAA failures

Retreatment of DAA failures with resistance

SVR12: 96% GT1a; 100% GT1b; 95% GT3

GT3 100% SVR (14/14)
Any way you slice it:
no significant impact of pre-treatment RASs

“Resistance” outside of drug selection
In vitro activity: "old" vs. "new"

<table>
<thead>
<tr>
<th>NS3 PI (nM)</th>
<th>GT1a</th>
<th>GT1b</th>
<th>GT2a</th>
<th>GT3a</th>
<th>GT4a</th>
<th>GT6a</th>
</tr>
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<tbody>
<tr>
<td>Paritaprevir</td>
<td>1.0</td>
<td>0.21</td>
<td>5.3²</td>
<td>19</td>
<td>0.09</td>
<td>0.68</td>
</tr>
<tr>
<td>Simeprevir</td>
<td>13</td>
<td>9.4</td>
<td>15</td>
<td>472</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Asunaprevir</td>
<td>4.0</td>
<td>1.2</td>
<td>230</td>
<td>1162</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Grazoprevir</td>
<td>0.38</td>
<td>0.87</td>
<td>1.3</td>
<td>36</td>
<td>1.2</td>
<td>0.89</td>
</tr>
<tr>
<td>Glecaprevir</td>
<td>0.85</td>
<td>0.94</td>
<td>2.7²</td>
<td>1.6</td>
<td>2.8</td>
<td>0.86</td>
</tr>
<tr>
<td>Voxilaprevir</td>
<td>3.9</td>
<td>3.3</td>
<td>3.7</td>
<td>6.1</td>
<td>2.9</td>
<td>1.5</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>NSSA (pM)</th>
<th>GT1a</th>
<th>GT1b</th>
<th>GT2a</th>
<th>GT2b</th>
<th>GT3a</th>
<th>GT4a</th>
<th>GT5a</th>
<th>GT6a</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ombitasvir</td>
<td>14</td>
<td>5</td>
<td>12</td>
<td>4</td>
<td>19</td>
<td>2</td>
<td>3</td>
<td>366</td>
</tr>
<tr>
<td>Daclatasvir</td>
<td>22</td>
<td>3</td>
<td>13,000</td>
<td>NA</td>
<td>530</td>
<td>13</td>
<td>5</td>
<td>74</td>
</tr>
<tr>
<td>Ledipasvir</td>
<td>31</td>
<td>4</td>
<td>21,000</td>
<td>16,000</td>
<td>168,000</td>
<td>390</td>
<td>150</td>
<td>1100</td>
</tr>
<tr>
<td>Elbasvir</td>
<td>4</td>
<td>3</td>
<td>3000</td>
<td>20</td>
<td>3</td>
<td>1</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Velpatasvir</td>
<td>12</td>
<td>15</td>
<td>9</td>
<td>8</td>
<td>12</td>
<td>9</td>
<td>75</td>
<td>6</td>
</tr>
<tr>
<td>Pibrentasvir</td>
<td>2</td>
<td>4</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>3</td>
<td></td>
</tr>
</tbody>
</table>

**NSSB nucleotide polymerase inhibitors** have consistent pangenotypic activity (sofosbuvir)

HCV genetic diversity and impact on DAAs

**GT6: LDV/SOF 12wks**
- 64% SVR (25/39)
  - 92% 6c-l
  - 6a: 10,000x EC50 1a
  - 250x EC50 6a

**France**
- 27 GT4r DAA failures
  - 24/27 non-pan geno regimens
  - 5 S282C/T

**GT4: LDV/SOF 12wks**
- 87% SVR (261/300)
  - 4r: 53% (27/48)
  - 4other: 93%

**GT1- non a/b:**
- 75% SVR (22/29)
  - 18 novel GT1 subtypes
  - K24G/S, L31M, H58P RASs

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- 75% SVR (22/29)
  - 18 novel GT1 subtypes
  - K24G/S, L31M, H58P RASs

**GT1- non a/b:**
- 75% SVR (22/29)
  - 18 novel GT1 subtypes
  - K24G/S, L31M, H58P RASs
GT3 non-3a subtypes and DAA resistance

- Subtype 3b- rare in registrational trials for all DAA regimens
- Prevalent SE Asia, China: Thailand 9.7%, Myanmar 29.7%

VEL/SOF GT3b (n=42)
76% SVR12
50% (7/14) cirrhosis
Wei L. Lancet Gastro Hepatol 2019

Back to Elimination
Global HCV Cascade

Egypt: from worst to first in 5 years?

Highest HCV prevalence in the world: ~10% +Ab, 7% +RNA → 5.5 million

2014: National treatment program

Total: 1,545,318
Egypt: First Country to Eliminate HCV?

National Screening program OCT18

3 phases
4,000-6,000 sites
12,000 trained
Medical facilities/mobile units

Since rollout:
28.8 million screened (78%)
1.2 million seropositive (4.1%)
- 860,000 viremic (3.0%)
$26/viremic case identified

Esmat et al. Lancet Gastroenterol Hepatol. 2018

VA: Shining US Example

VA has screened ~85% of 2.9 million veterans in the HCV birth cohort

Prevalence
• 2000: 19.2%
• 2018: 1.5%

Veterans awaiting treatment

Data as of 1 January 2019

JAN-JUN 2016: 22,463
JUL-DEC 2018: 5,508

168,708
28,049
Key issues and populations to address in elimination

- **Cost and Access**
- **Providers**
- **HCV Elimination**
- **Awareness and Identification**
- **High prevalence and transmitting populations**

- **Corrections**
  - PWID
  - HIV + MSM

Medicaid: Restrictions and Lack of Expansion

- **No Restrictions**
- **Chronic HCV**
- **F1**
- **F2**
- **F3**
- **F4**

- **Adopted and Implemented**
- **Adopted but Not Implemented**
- **Not Adopted**

https://www.kff.org/medicaid/issue-brief/status-of-state-medicaid-expansion-decisions-interactive-map


Abd US $390  FibroScan $436 Genotype $450-600
The cost of HCV medications

<table>
<thead>
<tr>
<th>Regimen</th>
<th>SVR rates</th>
<th>WAC Price</th>
<th>Cost per SVR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pegaspars + Ribavirin x 48 weeks¹</td>
<td>41%</td>
<td>$41,758</td>
<td>$101,849</td>
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<tr>
<td>Telaprevir + PegIFN + Ribavirin x 24 weeks²</td>
<td>75%</td>
<td>$86,843</td>
<td>$115,791</td>
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<tr>
<td>Sofosbuvir + PegIFN + Ribavirin x 12 weeks</td>
<td>90%</td>
<td>$94,421</td>
<td>$104,912</td>
</tr>
<tr>
<td>Sofosbuvir + Ledipasvir x 8 weeks</td>
<td>94%</td>
<td>$63,000</td>
<td>$67,021 ($36,191)²*</td>
</tr>
<tr>
<td>Sofosbuvir + Ledipasvir x 12 weeks</td>
<td>99%</td>
<td>$94,500</td>
<td>$95,054 ($51,545)²*</td>
</tr>
</tbody>
</table>

Early 2016 estimates

Incident HCV in the US
Continues to go in the wrong direction!

- 14 states with CDC funding for enhanced surveillance
- 2017: 5.6 cases/100,000 in West Virginia [1/100,000 Nationally]

2017
44,300 acute cases (35,000-151,100)
The “new” HCV epidemic

<table>
<thead>
<tr>
<th>Year</th>
<th>Adams</th>
<th>Arapahoe</th>
<th>Denver</th>
<th>Douglas</th>
<th>Jefferson</th>
<th>5-County Metro</th>
<th>Colorado</th>
</tr>
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<tbody>
<tr>
<td>2007</td>
<td>23</td>
<td>26</td>
<td>54</td>
<td>4</td>
<td>22</td>
<td>129</td>
<td>345</td>
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<tr>
<td>2008</td>
<td>38</td>
<td>18</td>
<td>49</td>
<td>5</td>
<td>21</td>
<td>131</td>
<td>368</td>
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<td>2009</td>
<td>15</td>
<td>18</td>
<td>47</td>
<td>8</td>
<td>20</td>
<td>108</td>
<td>306</td>
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<td>2010</td>
<td>18</td>
<td>22</td>
<td>50</td>
<td>4</td>
<td>16</td>
<td>110</td>
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<td>2011</td>
<td>20</td>
<td>20</td>
<td>42</td>
<td>9</td>
<td>16</td>
<td>107</td>
<td>332</td>
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<td>2012</td>
<td>24</td>
<td>21</td>
<td>44</td>
<td>4</td>
<td>24</td>
<td>117</td>
<td>375</td>
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<tr>
<td>2013</td>
<td>24</td>
<td>28</td>
<td>46</td>
<td>12</td>
<td>21</td>
<td>131</td>
<td>408</td>
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<td>2014</td>
<td>25</td>
<td>45</td>
<td>65</td>
<td>15</td>
<td>38</td>
<td>188</td>
<td>537</td>
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<tr>
<td>2015</td>
<td>25</td>
<td>37</td>
<td>76</td>
<td>13</td>
<td>43</td>
<td>194</td>
<td>622</td>
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<tr>
<td>2016</td>
<td>54</td>
<td>70</td>
<td>126</td>
<td>14</td>
<td>53</td>
<td>317</td>
<td>928</td>
</tr>
</tbody>
</table>

* Includes both acute and chronic cases, no duplicate individuals.
Age at time of diagnosis was 29 or younger
These numbers do not reflect those diagnosed in a state or federal prison.

New and expanded screening approaches are needed!

- Unidentified infections are likely in those not engaged in routine (primary) medical care and, increasingly, outside the birth-cohort

- **Screening in Emergency Departments**
  - Alabama (birth-cohort): 11% seroprevalence
  - 16.8% public/Medicaid
  - 16.9% uninsured
    - Baltimore (>17 yrs): 13.8% seroprevalence
    - Cincinnati (>18 to ≤64yrs): 13.9% seroprevalence
- **Common themes**:  
  1. Birth-cohort + risk-based screening missed up to 25% of infections  
  2. Most (~70%) unaware of HCV infection
Universal screening for HCV- it’s coming

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Average Lifetime Healthcare Cost</th>
<th>Life Expectancy</th>
<th>Quality-Adjusted Life Expectancy</th>
<th>Life Expectancy</th>
<th>Quality-Adjusted Life Expectancy</th>
<th>Life Expectancy</th>
<th>Quality-Adjusted Life Expectancy</th>
<th>Proportion Identified Prior to Cirrhosis</th>
<th>Proportion with HCV-Attributable Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard Care</td>
<td>$207,760</td>
<td>81.319</td>
<td>74.476</td>
<td>69.888</td>
<td>62.431</td>
<td>67.157</td>
<td>58.162</td>
<td>66.5</td>
<td>27.0</td>
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<tr>
<td>Test ≥40</td>
<td>$207,680</td>
<td>81.326</td>
<td>74.482</td>
<td>70.44</td>
<td>62.958</td>
<td>67.079</td>
<td>58.918</td>
<td>75.4</td>
<td>22.1</td>
</tr>
<tr>
<td>Test ≥50</td>
<td>$207,900</td>
<td>81.327</td>
<td>74.483</td>
<td>70.517</td>
<td>62.994</td>
<td>68.136</td>
<td>59.070</td>
<td>76.5</td>
<td>21.4</td>
</tr>
<tr>
<td>Test ≥10</td>
<td>$207,900</td>
<td>81.327</td>
<td>74.484</td>
<td>70.564</td>
<td>63.038</td>
<td>68.200</td>
<td>59.130</td>
<td>76.0</td>
<td>21.3</td>
</tr>
</tbody>
</table>

ICER (≥ 18): $28,000/QALY [dominated other strategies]

256,000 additional infections identified
280,000 additional persons cured

Barocas J. CID 2018.

The Arrival of Universal Screening

Recommendations for One-Time Hepatitis C Testing

<table>
<thead>
<tr>
<th>Population</th>
<th>Recommendation</th>
<th>Grade (What’s This?)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults ages 18 to 79 years</td>
<td>The USPSTF recommends screening for hepatitis C virus (HCV) infection in adults ages 18 to 79 years.</td>
<td>B</td>
</tr>
</tbody>
</table>

Draft USPSTF HCV Universal Screening Recommendation

HCV testing and linkage in Denver Adult Probations

Cascade of HCV in probationers seen at DH

Colorado prisoners reach settlement to get $41 million for hepatitis C treatment

By KIRK MITCHELL | kmitchell@denverpost.com | The Denver Post
PUBLISHED: August 28, 2018 at 2:15 pm | UPDATED: August 29, 2018 at 10:46 am
HCV testing and treatment in PWID: ETHOS engage

1001 PWID across 15 sites

TrapC (Iceland): Homeless status only factor associated with lack of SVR (RR: 2.42; 67% SVR)
- 72% on OST
- 57% excessive EtOH

Male gender and current OST (aOR 1.76) associated with treatment uptake

Fall in HCV incidence with DAA treatment in HIV + MSM: London 2013-2018

256 acute HCV cases
- 211 first infections
- 45 re-infections
Impaired access to DAAs may be hindering progress

60 MSM with acute HCV infection in London
Source of access to DAAs
- via NHS England: 10/49 (20%)
- via clinical trial: 15/49 (31%)
- generic medication purchased online (10 SOF + LED, 4 SOF + VEL, 3 SOF + DAB): 23/49 (47%)
- via health services abroad: 1/49 (2%)
Median time to access to DAAs according to source, days (IQR)
- via NHS: 278 (174-417)
- via clinical trial: 132 (108-155)
- generic medication purchased online: 114 (75-201)
SVR at 8 wk: 49/49 (100%)
SVR at 12 wk: 49/49 (100%)

Girometti N. J Viral Hep 2018

Update recommendation for management of Acute HCV infection

Recommendations for Medical Management and Monitoring of Acute HCV Infection

<table>
<thead>
<tr>
<th>RECOMMENDED</th>
<th>RATING</th>
</tr>
</thead>
<tbody>
<tr>
<td>After the initial diagnosis of acute HCV with viremia (defined as quantifiable RNA), HCV treatment should be initiated without awaiting spontaneous resolution.</td>
<td>I, B</td>
</tr>
<tr>
<td>Counseling is recommended for patients with acute HCV infection to avoid hepatotoxic insults, including hepatotoxic drugs (eg, acetaminophen) and alcohol consumption, and to reduce the risk of HCV transmission to others.</td>
<td>I, C</td>
</tr>
<tr>
<td>Referral to an addiction medicine specialist is recommended for patients with acute HCV infection related to substance use.</td>
<td>I, B</td>
</tr>
</tbody>
</table>

Treat as for chronic HCV...for now.
Treatment of Acute HCV Infection in HIV+ MSM

SVR12 per protocol 87%²
2 LTFU
1 reinfection

Viral Load, by Outcome²

Individual Patients, by Outcome

G/P for Acute HCV

Recent HCV infection (<12 mo)
- 30 participant- G/P for 6 weeks
  - A5380
  - Glecaprevir/pibrentasvir Fixed-dose Combination Treatment for Acute Hepatitis C Virus Infection (PURGE-C)

4 weeks G/P
<6mo infection
HIV+ and HIV-

David Wyles, M.D.
Treating Acute HCV in HIV MSM at high risk for reinfection is cost saving

- Model assumptions based on Dutch HCV epidemic
- Incidence 1.2/100 p-y, reinfection 15/100 p-y

<table>
<thead>
<tr>
<th>Scenario</th>
<th>HCV infections averted at 40yr</th>
<th>HCV Prevalence reduction at 20yr</th>
<th>Total costs, Euro's (millions)</th>
<th>QALY x 1000</th>
<th>Incremental costs Euro's (millions)</th>
<th>Incremental QALYs</th>
<th>ICER</th>
</tr>
</thead>
<tbody>
<tr>
<td>F2</td>
<td>-</td>
<td>-</td>
<td>€ 98.4</td>
<td>331.3</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>F0 acute</td>
<td>7457</td>
<td>97%</td>
<td>€ 68.3</td>
<td>334.7</td>
<td>-€ 30.0</td>
<td>3425</td>
<td>cost saving</td>
</tr>
<tr>
<td>F0 chronic</td>
<td>7070</td>
<td>96%</td>
<td>€ 75.1</td>
<td>334.6</td>
<td>€ 6.9</td>
<td>-47</td>
<td>dominated</td>
</tr>
</tbody>
</table>

NYC HIV+MSM HCV Re-infection data


304 cases
- 37 re-infections
- 6 second re-infections
Median f/u 2.2 yrs

Re-infection 4.4/100 p-y
2nd Re-infection 8.7/100 p-y
Evidence of increasing transmission to HIV- MSM

• Risks as expected
  • Chemsex, traumatic and group sex
• Dramatic increase in HIV-MSM in 2017

Risk to micro-eliminations from re-introduction outside cohorts?
On track to meet 2030 HCV elimination goals?

First RCT of Candidate Preventative HCV Vaccine
Prime: ChAd3-NS  Boost: MVA-NS
• HCV 1b vector NS antigens)
Concluding thoughts…

• Aggressive goals for HCV elimination have been put forth
  • Right now only a handful of countries are on track
• Dramatic progress can be made in a short time with integrated
  (National) screening and treatment programs
  • Universal access to therapy
• Fragmented healthcare system and lack of political will, along with
  inadequate treatment of substance use will hamper HCV elimination
  efforts in the US
  • Still that doesn’t mean we can pursue micro-elimination efforts
• Drug resistance after initial DAA failure unlikely to have a major
  impact
  • More data is needed on subtypes not well represented in clinical trials

Acknowledgements

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